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DISEASES OF THE NERVOUS SYSTEM

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DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

BAL in the Treatment of Neurological Syndromes

HARRY M. SALZER, M.D.
Cincinnati, Ohio

In the opinion of some neurologists, the neuropathies are primarily a biochemical disorder of the neurone resulting from abnormal cell metabolism, the metabolic malfunction arising from derangement in one or more enzyme systems. Therefore if enzymatic equilibrium could be restored, the dysfunction should rapidly disappear.

Accordingly British Anti-Lewisite abbreviated to BAL was used because of its success in restoring enzymatic equilibrium in arsenic, mercury, antimony, and cadmium intoxication. Heavy metals have an affinity for sulfhydryl radicals in both organic and inorganic molecules. In heavy metal poisoning the noxious agent combines with the sulfhydryl component of cellular protein regulating carbohydrate and fat metabolism.

The thiols, for example cysteine and glutathione, have greater affinity for metals than the cellular thiol and the dithiols surpass the thiols in this capacity. BAL, a synthetic propanol, is the best of the dithiols, because it contains two sulfhydryl radicals and it was found to be capable of removing metal from enzyme proteins by forming a more stable insoluble non-toxic compound which can be rapidly excreted.

Likewise the toxic effect of BAL results from this affinity for too great a dose can remove from the cell not only the metallic poison but also needed copper, zinc, iron and magnesium.

The suggestion that BAL treatment be used in severe peripheral neuropathies was first made by Dr. J. M. Nielson of Los Angeles and the first article to appear on its clinical application was one by Furmanski[1] in September 1948.

Furmanski reported four cases of severe neuropathy which had failed to respond to the usual oral and parenteral treatment of liver extract and vitamin in therapeutic doses. A 10% solution of BAL was used in an amount ranging from 1.5 mg. to 3 mg./kg. per day.

Briefly in Furmanski's first case of what seemed to be one of nutritional deficiency neuritis and in which there had been progression for two months in face of adequate vitamin therapy, within ten days after administration of BAL the patient had improvement in all muscular strength. In the second case, one of mixed nutritional deficiency and alcoholic peripheral neuropathy, no improvement was noted in three months of routine vitamin therapy but after nine days of treatment with BAL, signs and symptoms disappeared. In the other two cases similar results were noted, both of them improving within a few days.

A few other reports have appeared on the use of Dimercaptopropanol or BAL. Creaturo[2] reported a case of Guillain-Barré syndrome treated with BAL with increased strength in the legs occurring in four days after administration of BAL.

In June, 1950, Dr. J. M. Nielsen[3] reported treatment of ten cases of Guillain-Barré syndrome with BAL. Nine improved when BAL was given and relapsed when it was discon-

Presented before the Cincinnati Society of Neurology and Psychiatry.

tinued. A progressive downhill course in several patients seemed to be abruptly reversed by the administration of BAL. One diabetic patient showed no improvement.

This paper presents the results of BAL therapy in six cases of Guillain-Barré syndrome, in four miscellaneous cases, and in five cases of encephalo-myelo-radiculitis.

Case 1—A 43 year old punch press operator referred by Dr. A. Renz was seen on April 18, 1949. On March 1, 1949 he had sore throat, pain in the shoulders, back, neck and over the vertex. He failed to improve, in fact was worse with Penicillin therapy and one week later he could hardly walk on account of weakness of the lower extremities. The findings were those of bilateral facial palsy and there was severe weakness of abduction at the shoulders whereas the grips were excellent. Straight leg raising against resistance was weak. A lumbar puncture was refused. On a clinical basis a diagnosis of Guillain-Barré syndrome was made. The patient received ten injections of BAL in doses of 225 mg. (2¼ c.c.) daily. Upon neurological recheck May 4, 1949, six days after treatment was terminated, the patient felt improved. Abduction at the shoulders and flexion at the hips were strong. He was able to elevate the eyebrows which he could not do before. The teeth could be shown slightly on the left and he was just able to close the right eyelids.

Case 2—A 42 years old laborer referred by Dr. H. Dreskin was admitted to the hospital on September 18, 1949 with a history of progressive difficulty in walking for two weeks, so that on admission he could not walk without assistance. On examination there was loss of all deep reflexes and weakness of the thighs. The arms were weak but to a lesser extent. On the day of admission the C.S.F. protein was 120 mg. There were no cells and the C.S.F. serology was negative. A diagnosis of Guillain-Barré syndrome was made. On September 23, 1949, BAL was started in doses of 180 mg. (1.8 c.c.) q.i.d. for three days, 180 mg. (1.8 c.c.) b.i.d. for one day, and 180 mg. (1.8 c.c.) once a day for ten days. BAL was given for fourteen days being discontinued on October 7, 1949. Twenty-four hours after treatment was started there was increased motor power in the lower extremities. The grips had improved. On September 30, 1949, one week after treatment began, he stood without support but could not walk. Muscular strength then seemed almost normal when he was in bed for testing. The eighth treatment day 10 to 15 steps could be taken without support, and the eleventh day of treatment he was described as recovered. A C.S.F. protein of 54 mg. was recorded on this date. Other therapy during the time consisted of Solu B, I.V. for two days but it was stopped three days before BAL was begun. During the entire hospital stay he received three therapeutic vitamin capsules per day.

Case 3—A 31 year old housewife, three and one-half months pregnant, referred by Dr. H. Wiley, was admitted to the hospital on December 21, 1949 and she was examined neurologically on December 25, 1949. She gave a history of having peripheral numbness and weakness in all extremities and severe back pain. On examination there was weakness of the left face in all areas and weakness at the right mouth corner only. There was proximal weakness of all extremities. Pain sensation was reduced below D-8. All the deep reflexes were absent. The C.S.F. protein was 120 mg. and there were three R.B.C. A diagnosis was made of Guillain-Barré syndrome. BAL was started on December 26, 1949 and continued for twelve days as follows: 225 mg. (2¼ c.c.) b.i.d. for five days, 225 mg. (¼ c.c.) once a day for seven days. Liver extract was not started until January 1, 1950. On December 27th, twenty-four hours after BAL was administered, there was improved power at the shoulder girdle. Back pain had decreased. Weakness at the hips and the facial weakness remained the same. On the second and third days of treatment, the right face was more involved but the arms remained strong, especially at the shoulders, and the hips were slightly stronger. On December 30th, the fourth treatment day, the arms were generally strong. Straight leg raising was possible to thirty degrees on the right and fifteen degrees on the left. The sensory level had moved from D-8 to the lower third of the legs. The facial palsy continued. On the fifth day of treatment with BAL, December 31st, there was slight wrinkling of the forehead. On the sixth treatment day, January 1, 1950, the left facial weakness had improved and power in the arms was excellent. On January 6th, the eleventh day of treatment, the left face was much improved. By January 11th, the fourth day after BAL was discontinued, there was bilateral increase in facial movement. Straight leg raising was still thirty degrees on the right and fifteen degrees on the left. On January 16th, nine days after BAL was stopped, the facial palsy had recovered and on January 27th she was discharged with improvement maintained.

Case 4—A 13 year old school boy referred by Dr. C. Wyler was seen in the hospital on May 15, 1951. He complained of weakness of both legs and paralysis of the left side of the face. The gait was slow on account of pain in the posterior thighs. On neurological examination there was left peripheral seventh nerve palsy. Symmetrical proximal weakness was found upon abduction of the shoulders and extension at the elbows. There was bilateral weakness of flexion at the hips and knees along with bilateral partial foot drop. The arm reflexes were reduced and the lower extremity reflexes were absent. The C.S.F. protein was 100 mg. and there were three white and eight red cells. A diagnosis of Guillain-Barré syndrome was made. BAL in doses of 150 mg. (1½ c.c.) was given for five days beginning May 15, 1951. On May 22nd, three days after BAL was stopped, there was left facial improvement so that he could purse the lips and close the eyelids. Ab-

duction at the shoulders was strong. Straight leg raising could be carried out to sixty degrees and it had improved against resistance. Foot drop was less. He was discharged on May 23, 1951 with maintained improvement.

Case 5—An office manager, 45 years old, referred by Dr. H. Felson, was seen first in the hospital on March 24, 1952. He gave a history of having had a respiratory infection the last week of February, 1952. On March 7, 1952 he developed tingling in the fingers and heaviness of the feet and on climbing stairs he noticed weakness of the lower extremities. On examination there was weakness at the shoulder girdle bilaterally. He could not stand on either foot singly and there was weakness of flexion at the hips. The C.S.F. protein was 71 mg. and there were two W.B.C. He was discharged from the hospital on March 29, 1952, treatment having been deferred on account of a chronic duodenal ulcer. On April 17, 1952, there was still weakness of the legs and the feet hit the floor without spring. There was weakness of extension at the wrists, of flexion at the hips, and of dorsiflexion of both feet. There was unsteadiness on either foot singly. A diagnosis of Guillain-Barré syndrome was made. BAL, 225 mg. (2¼ c.c.), was administered for five days beginning April 17, 1952. Nausea occurred after the first injection but was relieved by Resinat and Tricreamalate. On April 18th, after the second injection, there was slight nausea but less than the previous day because this time he received Resinat and Tricreamalate first. That day he could stand slightly better on the left foot singly, and there was questionable improvement of extension at the wrists. On May 8th, he felt that strength had improved after the BAL injections. He was walking better, could stand on either foot singly, extension at the wrist was weak on the right only. Other power in the arms was excellent. Straight leg raising could be accomplished to seventy-five degrees and flexion at the hips against resistance could not be opposed. All the deep reflexes remained absent. When seen on May 14th and 28th by the family physician, he was reported as having good strength.

Case 6—A 30 year old housewife referred by Dr. M. Osher was seen on July 18, 1949. On July 6, 1949 she had a normal delivery and was well the following week in the hospital and for three more days at home. On July 15th, she developed pain in the left buttock, left posterior thigh, especially on sitting, and the pain was sufficient to keep her awake. Weakness of the left lower extremity was noticed and she had bitemporal headache, occipital pain and severe fatigue. Examined July 18th, the grips were weak and so was abduction at the shoulders and flexion and extension at the elbows and wrists. In the lower extremities there was weakness of flexion at the hips and weakness of flexion and extension at the knees, especially on the left. Dorsal and plantar flexion at the ankles was strong and toe wiggle was fair. The left sciatic notch was tender as was the sciatic nerve. A diagnosis of Guillain-Barré syndrome was made on a clinical basis, lumbar puncture having been refused. 225 mg. (2¼ c.c.) of BAL was given at once. Re-examined the next day, motor power was found to be almost normal. Pain, which on July 18th was so severe that she could not sit on the left buttock, was gone on July 19th. The next morning she had nausea and faintness after BAL and no further injections were given.

Four miscellaneous cases were treated with BAL without help, as follows:

Case 7—Multiple sclerosis, was treated with 225 mg. (2¼ c.c.) daily for ten days.

Case 8—Myasthenia gravis, was treated with 200 mg. (2 c.c.) daily for eleven days.

Case 9 and 10—Amyotrophic lateral sclerosis, one was treated with 225 mg. (2¼ c.c.) daily for twelve days and the other for ten days.

Five cases of encephalo-myelo-radiculitis were treated with BAL. These cases did not albumino cytological dissociation.

Case 11—A 39 year old clerk referred by Dr. H. Felson was seen April 14, 1949. He gave a history that on April 7th fatigue was present and on April 8th he was confused. On April 9th he ran a temperature of 101. Two days later, on April 11th, severe hyperalgesia was present in the left upper chest. On April 14th he had tingling from the knees to the hips and could not stand a sheet or a shirt over his chest. Examined on April 14, 1949, pain and temperature sensations were found to be reduced from D-2 to 8, and pain sensation was reduced in the entire right lower extremity. Anteflexion of the head produced pain along the costal margin. X-rays of the spine were negative. A spinal puncture was refused. A diagnosis was made of encephalo-myelo-radiculitis. 200 mg. (2 c.c.) of BAL was given daily for five days. By the fourth day the paresthesia was gone, the patient felt well and treatment was discontinued.

Case 12—A 44 year old, used car salesman, referred by Dr. I. Claybon was seen on January 19, 1949. He had fatigue, headache, blurred vision, weakness of the legs and urinary retention. There was weakness of abduction at the shoulders and the grips were weak. The knee jerks were reduced, left plantar response was extensor and the right was flexor. There was a sensory loss to D-4. The C.S.F. had 82 lymphocytes and a total protein of 63 mg. A diagnosis of encephalo-myelo-radiculitis was made. On C.S.F. re-examination in August, 1949, there were 5 RBC and a total protein of 33 mg. BAL, 225 mg. (2¼ c.c.) once a day, was administered for the first five days in September without improvement.

Case 13—The patient, referred by Dr. J. Freiberg and Dr. W. Phillips, was a 40 year old housewife seen on November 20, 1951. November 7, 1951 through November 9th, the patient had an upper respiratory infection. On November 10th she no-

ticed numbness on the left, from the chest down. There was weakness of the left lower extremity, soreness of the left buttock and aching of the left knee. She had fatigue and on November 17th developed staggering, weakness, tingling of the right lower extremity and to the upper abdomen. She was also emotionally upset. The deep tendon reflexes were hyperactive and the abdominals were absent. Plantar responses were not up or down. From below pain was lost on the left to L-1 and reduced to D-2. There was foot drop on the right, weakness of flexion at the right hip and of dorsiflexion at the right ankle. The gait was of the right spastic hemiparetic type. X-rays of the spine were negative. The C.S.F. protein was 47 mg. and there were 2 lymphocytes. A diagnosis was made of encephalo-myelo-radiculitis. On December 7, 1951, two and one-half weeks later, there was, in addition, grade 2 ataxia on the heel to shin tests, the Romberg test was two plus and there was a wide based ataxic gait.

BAL, 225 mg. (2¼ c.c.), was administered once a day for five days beginning December 8th. On December 12th she felt dramatically better. On December 14th the left thigh sensation had returned; straight leg raising improved from 60 degrees right, and 75 degrees left, to 90 degrees. The upper abdominal reflexes had returned. Another course of BAL, 225 mg. (2¼ c.c.), once a day for five days was given. The patient walked without a cane on January 1, 1952. Pain sensation had returned by January 3rd. When reexamined on January 18, 1952, the Romberg test was only one plus and the ataxic heel to shin tests had become almost normal. The reflexes were still hyperactive but the gait was almost normal. On March 10, 1952, the Romberg test was negative; the heel to shin tests were entirely normal; the plantars were normally flexor.

Case 14—A 45 year old social worker referred by Dr. S. Goldblatt was seen on February 3, 1951. In November, 1950 a cerebro spinal fluid check was made because the patient had had C.N.S. lues in 1948 and treatment with Penicillin had been successful. In November, 1950 the C.S.F. Kohlmer was anticomplementary, the total protein was 76 mg., the gold curve was 0-0, and there were 15 WBC. On December 12, 1950, the patient developed bilateral quivering of the gluteal muscles. She was given Aureomycin by the referring physician. On December 16, 1950 there was quivering of the entire body below the hips. She received hormonal therapy, phenobarbital and Nembutal and the quivering decreased. A biopsy of the cervix was negative. In early January, 1952, the C.S.F. protein was 64 mg. and there were 17 cells. The Wassermann was negative and the gold curve was 0-0. The referring doctor gave her 800,000 units of Penicillin daily until January 29th without improvement in the quivering. Treatment with Aureomycin and Chloromycetin had not been helpful, and injections of calcium were of no benefit. The quivering would awaken her and the feet might straighten out. Slight tingling in the left groin was present. She could walk only with great difficulty when the gluteal tremor was present. On examination there was spasm of the right calf and tonal increase at the right hip. The knee and ankle jerks were normal and the plantar responses were flexor. There was periodic contraction of both gluteal and lumbar muscles to L-2. A diagnosis was made of probable virus radiculitis. BAL, 225 mg. (2¼ c.c.), was administered daily for six days. The patient reported great improvement. When BAL was stopped the patient became worse again but the referring physician did not give further doses of BAL.

Case 15—An eight year old school boy, referred by Dr. S. Okrent, was examined on June 3, 1952. On May 13, 1952 the patient had severe headache lasting for two and one-half days. He felt well the next three days but had vomited from May 16th to May 19th. Starting May 19th he had diarrhea until May 21st. During the first week of the illness the patient had enuresis three times. The temperature had been 101 and the pharynx was injected. On May 23, 1952, the patient was irritable, weak, laughed too much, and tended to fall forward or backward. He could not talk above a whisper. Beginning May 31st he held the left arm flexed and stiff and on June 2nd he had intermittent twitching of the right shoulder. When examined June 3rd, there was masked facies, monotonous voice, stare, cogwheel tone on the left, slow initiation of power, especially on the left, and failure to perform rapid alternating movements well, especially on the left. The left arm was held flexed and there was loss of associated movement on the left. He had lateral-pulsion to either side but not pro- or retropulsion. The Myerson reflex was positive. A lumbar puncture was refused. The case was diagnosed as one of post encephalitic left hemi-Parkinson's syndrome. The referring pediatrician gave the patient five injections of BAL, the first day 70 mg. (0.7 c.c.), the second day 90 mg. (0.9 c.c.), and the third to the fifth day 100 mg. (1 c.c.) daily. The pediatrician reported the patient was "upset" by the injections but was unable to clarify that, other than to state the patient disliked the injections. The patient "may have had nausea" but definitely did not vomit. Two weeks aftr the injections the patient improved abruptly, becoming entirely normal.

In this last case improvement might have taken place as the result of termination of the encephalitic process and cessation of associated cerebral edema. Because improvement occurred two weeks after BAL therapy, one can not use post hoc propter hoc reasoning.

In an editorial note in the *1950 Yearbook of Neurology and Psychiatry,* Dr. Roland Mackay[4] remarked:

"The treatment of infectious polyneuritis

or the Guillain-Barré syndrome with 2-3 Dimercaptopropanol (BAL) is an interesting experiment. . . . One need only warn that therapeutic tests are not easy to interpret in conditions which often resolve spontaneously."

Summary

This study has been a clinical one, and the virus etiology in these cases has been suspected but not proved. It is the author's impression that BAL has been helpful in the six cases of Guillain-Barré syndrome, in four of the five cases of encephalo-myelo-radiculitis, and not at all in multiple sclerosis, myasthenia gravis, and amyotrophic lateral sclerosis.

REFERENCES:

1. Furmanski, A. R.: BAL Therapy of Severe Peripheral Neuropathies, *Arch. Neurology and Psychiatry,* Vol. 60:270, (Sept.) 1948.
2. Nielsen, J. M.: Treatment of Neuronitis With BAL, *Bull. Los Angeles Neurol. Soc.,* 15:61, (June) 1950.
3. Creaturo, N. E.: Infectious Mononucleosis and Polyneuritis (Guillain-Barré Syndrome): Report of Case of Facial Diplegia Treated With Two to Three Dimercaptopropanol (BAL).
4. Mackay, R. P.: Editorial Note, *Yearbook Neurology, Psychiatry and Neuro-Surgery:* 1950, page 114.

E. E. G. Changes During Administration of Carbon Dioxide

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and
THEODORE HILL, M.D.
South Bend, Indiana

A mixture of 30 per cent carbon dioxide and 70 per cent oxygen is being used in the treatment of certain psychiatric conditions. The physiological basis of this treatment is, however, obscure and theoretical. In an attempt to further elucidate the physiology involved, EEG's were obtained during the course of routine treatments.

Technique

A group of 37 young adults, most of whom had never had a previous treatment, were used as volunteer subjects. Electrodes were placed over the frontal, occipital, and temporal areas of the skull on both sides. Each lead was run to the same bilaterally connected ear lead. In 29 patients, a precordial lead was also used so that an EKG could be obtained simultaneously with the EEG. A control record was obtained with the patient supine; he then voluntarily hyperventilated for three minutes following which the EEG record was obtained for another two minutes or until such time after overbreathing that the record returned to its former pattern. After a five minute rest, and without moving the patient, a mask with an attached bag as a reservoir was applied over the face and nose and 30 per cent CO_2-70 per cent O_2 mixture of about 6 pounds pressure was administered. An EEG was obtained at the same time. The person administering the gas counted aloud the patient's respirations.

Results

A fairly constant EEG pattern was obtained during a treatment. This consisted of a short period of alpha, then loss of this alpha with a general decrease in the amplitude, followed by a fairly sudden appearance of high voltage, slow, predominantly 4 to 6 per second regular waves whose definition and amplitude increased in a crescendo, plateaued and then decreased more rapidly than they appeared. An irregular, low voltage, slow wave pattern was then noted which in some records seemed to differ from the low voltage pattern that immediately preceded the high voltage phase in that the former contained more delta and was more irregular. Finally, the pretreatment pattern reappeared. (Figure 1.) The EEG's which were obtained have been grouped into: (1) results of the total series, (2) results of those in which only 30 breaths of CO_2-O_2 mixture were given, (3) results of those in

From Neurology Section, V.A. Hospital, San Francisco, Calif., and Association for Mental Health, South Bend, Ind.

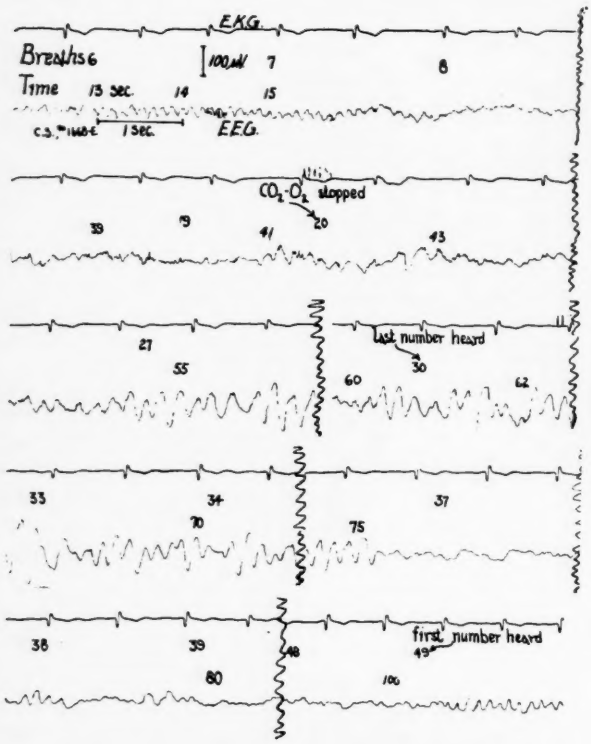

Figure 1. Portions from a record showing the entire sequence of changes: alpha, loss of alpha, high voltage 5/second slow waves ("build-up"), low voltage, irregular slow waves, and reappearance of the alpha. This particular tracing was chosen because of the minimal amount of artifact; however, it is atypical in that the "build-up" begins after the gas was stopped and there is not the usually greater amount of slowing after the "build-up" than before the "build-up."

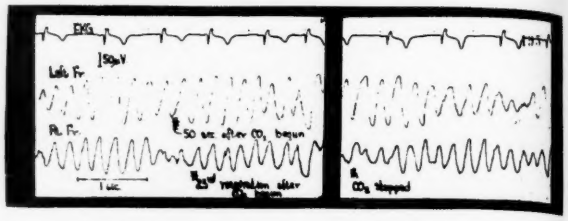

Figure 2. A very clear "build-up."

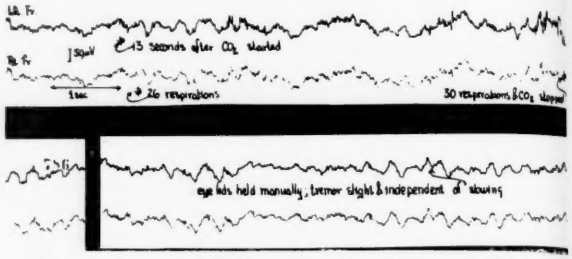

Figure 3. An E.E.G. showing some slowing and increase in voltage but not regular enough to be defined as a "build-up." The record is a continuous one except for about 0.4 second at the black line in the lower half of the figure.

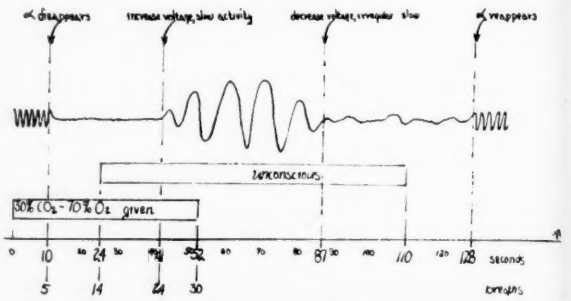

Figure 4. A "typical" E.E.G. response to 30% CO_2-70% O_2 based on the average obtained from our group that received 30 breaths of the gas.

which only 30 breaths of gas were given and there was a "build-up," and (4) those, where regardless of how much gas was given, there was a "build-up." We have used the term "build-up" to describe the appearance of not only high voltage, slow activity, but, rather to define a striking phenomenon during which these high voltage slow waves were well delineated, regular, sinusoidal and with definite limits. (Figures 2 & 3.) The time in seconds and in breaths required for each of the various parts of the EEG sequence have been tabulated (Table 1) and using the averages obtained from these a tracing of a "typical" record has been constructed. (Figure 4.) Because of several minor changes in our routine and the production of artifact during part of some of the records, each of the various phases of the EEG sequence that is tabulated does not represent the total number of EEG's that were obtained; for this reason, each entity in Table 1 has listed with it the number of records upon which the various averages were based. Therefore, where only several, or in some cases only one record is used to form an average, the statistical reliability must be very poor or nil. The various changes in the EEG will usually be discussed on the basis of the average; however, the range of each item is also given in Table 1.

1. *Total time the gas was given:* The average time that the CO_2-O_2 mixture was given was about the same in all the groups. It took about 50 to 52 seconds for the average patient to inhale 29 to 30 times. The range of the "no build-up" group was slightly greater than in the other groups; this is probably because these records were from patients who not infrequently exhibited but little change in the EEG during the treatment, so that the administration of the gas

was continued for a longer period of time. On the other hand, there were those in this particular group who became so frightened by the procedure that it had to be terminated earlier than usual. The shorter end of the range in the other groups can be accounted for by patients who exhibited a marked clinical effect—considerable tremor, rigidity, etc.—early in the course of treatment, or who had an early and marked "build-up" in the EEG which caused us to terminate the treatment early.

2. *Changes in alpha:* The time at which the alpha disappeared was, on occasion, difficult to determine because of the frequent loss of alpha when the mask was applied to the face (attention?) or because of the muscle artifact which appeared early in many cases; this artifact did not have to be marked in order to obscure the alpha. However, in those where changes could be seen, the alpha disappeared on the average in 10 to 15 seconds (5 to 7 breaths) after the treatment was begun. The alpha returned earlier if there was no "buld-up," reappearing in approximately 100 seconds after treatment was begun, as compared to 128 to 131 seconds when there was a "build-up."

3. *Changes in consciousness:* This was tested by asking the patient what was the last number that he heard, and then, the first number he heard when he again became aware of the counting. If the patient claimed he heard all the numbers, it was assumed that he did not lose consciousness. This is a common method used when the CO_2-O_2 mixture is given in the clinic; however, it is very unreliable. The answer given by the patient varied according to how soon he was quizzed about it after the treatment was over and it was easily changed by minimal suggestion. One reliable and intelligent patient claimed inability to hear any number between 20 and 70. He was eagerly looking forward to his release from military duty in five days; the statement "you have 50 more days" was used instead of the count "50" and this he heard while by the count method he was regarded as being unconscious. Another male patient who did not remember any count between 50 and 70 did recall hearing the statement "60 beautiful girls just walked into the Lab," which was used in the place of the count "60." However, using the count method as a guide for the loss and regaining of consciousness, the average patient was "unconscious" in 24 to 28 seconds (14 to 16 breaths). "Consciousness" was regained, on the average, within 110 seconds after the treatment was begun.

4. *High voltage, slow activity, and "build-up":* Only one out of 36 patients had no discernible increase in voltage or slowing of his basic rhythm; 29 of the remaining 35 patients had a "build-up." The average duration of the high voltage, slow activity in the group where it was not regular or sinusoidal enough to be classified as a "build-up" by our definition, was 21 seconds and the amplitude was 78 microvolts; this was decidedly less than the group that included a "build-up" where the average duration was 47 seconds and the average amplitude was about 128 microvolts.

5. *Relation of the EEG during treatment to the clinical manifestations:* Of the five apparent grand mal seizures noted in our series, one of the patients represented two of our experimental EEG's; he had a grand mal seizure each time. He had received a course of CO_2-O_2 treatment previously and it was observed that he had a grand mal seizure with almost every treatment; he was purposely chosen for the experimental series. During one of the treatments he had a considerable "build-up" but during the other experimental treatment, the EEG record was so full of artifact that the details could not be made out adequately. The control record before the first treatment was interpreted as borderline because of a small amount of scattered slowing whereas the control record before the second treatment was interpreted as normal. Another patient who also had a grand mal seizure with each treatment and hence was also purposely chosen for our experiment, had a convulsion during the experimental treatment, too. His record was so full of artifact that it could not be decided whether there was a "build-up" or not. Again, the control portion of the EEG was normal. The third patient *may* have had a convulsion; he did not have a "build-up." His convulsion (?) was not a typical tonic seizure, followed by clonic jerking, but there was such rigidity followed

by such tremor that we considered it to be possibly a grand mal seizure. The control portion of the record was mildly abnormal with a scattering of delta activity and poorly defined spiky activity. Of all those who had a convulsion, there was nothing in the readable parts of the treatment record that distinguished them from the other treatment records, although admittedly, the great amount of artifact that was obtained may have obscured some pertinent features.

6. *Relation between the pre-treatment (control) EEG's and the EEG's during treatment:* There were three abnormal pretreatment (control) EEG's in addition to another three which, though they had normal pre-hyperventilation records, had considerable nonfocal high voltage slow activity during hyperventilation which was sustained for more than a minute after the overbreathing stopped. There was no constant relationship between the pre-CO_2-O_2 EEG and any changes noted in the EEG during treatment.

7. *Changes in pulse rate during treatment:* The pulse rate was counted in 29 patients immediately before the treatment was begun, immediately after the treatment was terminated, and again when the "build-up" was at its height. There was no constant change in the pulse rate; it was the same before and after treatment in 2, it increased after treatment in 12, and it decreased after treatment in 15. Of interest was the presence of extrasystoles in five individuals during and immediately following treatment. There was no constant relationship between the direction of change of the rate of the pulse and the presence of extrasystoles.

Discussion

During 30 per cent CO_2-70 per cent O_2 treatment there is a fairly constant sequence of change in cerebral metabolism as measured by alterations in the pattern of the EEG. The averages we have used to compile our "typical" EEG response are based on figures with a considerable range. This is probably to be expected for Meduna[1] notes that the response may vary from treatment to treatment and from patient to patient during the course of a series of treatments. The loss of alpha and the appearance of a low voltage pattern is the EEG response to increased CO_2[2,3] and decrease O_2[4,5] tension. The most outstanding change in our "typical" EEG was the "build-up." Whether, when seen, this is a definite entity or merely a marked amount of the same slowing noted in several other records is not certain. However, it was so striking that we have considered it, at least tentatively, as a particular phenomenon. Meduna quotes Gibbs as describing 3 to 4 per second high voltage activity in the EEG during the "second phase (state of narcosis)" of a 30 per cent CO_2-70 per cent O_2 treatment; this began 6 to 12 respirations after the treatment was started, and continued for another 6 to 12 respirations. If this is the same change we have described as high voltage, slow activity and/or "build-up" it occurred later in our group. We did not compute the duration of high voltage, slow activity in terms of respirations but rather in seconds; in terms of seconds the duration of this phenomenon in our series was about the same as the time of onset of this change and hence the number of respirations are probably about the same; i.e., average about 23 to 24 breaths. The difference in time of the onset and duration of the slow activity between Meduna's and our group may be due to some differences in technique and may not represent anything more important than that. There is, however, another discrepancy and that is between the frequency of the slow activity noted by Gibbs—3 to 4 per second—and that most frequently seen in our series—4 to 6 per second.

The presence of extrasystoles in five patients suggests an increased cardiac irritability. This adds further confirmation to Meduna's[6] belief that heart disease is a contraindication to treatment.

Summary

1. EEG's of 37 persons given 30 per cent CO_2-70 per cent O_2 inhalations in a manner similar to that given in the treatment of certain psychiatric conditions was obtained in an attempt to further elucidate the physiological basis of this particular type of treatment.

2. A fairly characteristic pattern of change in the EEG was seen and has been discussed.

TABLE 1

			Total	*30 breaths*	*Total "build-up"*	*30 breaths "build-up"*	*Without "build-up"*
Total time CO_2-O_2 given	Average	(seconds)	52	52	50	52	46
	Range	(")	93-26	71-36	71-33	71-36	80-26
	No. entries	(")	38	18	27	15	8
	Average	(breaths)	29	30	29	30	26
	Range	(")	50-15	30-30	40-20	30-30	50-15
	No. entries	(")	37	18	27	15	8
Time & disappears	Average	(seconds)	12	10	11	10	14
	Range	(")	20-3	16-6	16-3	16-6	19-9
	No. entries	(")	21	9	16	8	4
	Average	(breaths)	6	5	5	5	7
	Range	(")	8-2	8-5	8-2	8-5	8-5
	No. entries	(")	21	9	5	8	4
Time consciousness lost	Average	(seconds)	28	24	28	24	24
	Range	(")	67-9	44-12	67-9	44-9	24
	No. entries	(")	24	14	22	13	1
	Average	(breaths)	16	14	16	14	17
	Range	(")	50-5	24-6	50-5	24-6	17
	No. entries	(")	24	14	22	13	1
Time consciousness regained	Average	(seconds)	126	110	105	110	115
	Range	(")	146-56	146-78	146-56	146-78	115
	No. entries	(")	21	12	20	12	1
Time onset increase voltage slow activity	Average	(seconds)	42	45	41	43	42
	Range	(")	81-0	81-0	81-24	81-24	80-0
	No. entries	(")	36	16	27	14	8
	Average	(breaths)	24	23	24	24	23
	Range	(")	58-0	36-0	58-13	34-13	36-0
	No. entries	(")	34	17	26	14	7
Duration of increase voltage, slow activity	Average	(seconds)	41	46	47	51	21
	Range	(")	93-0	88-0	93-10	88-19	64-0
	No. entries	(")	35	17	27	14	8
Amplitude of increase voltage, slow activity	Average	(M V)	120	116	134	125	78
	Range	(")	270-0	210-0	240-60	210-60	270-0
	No. entries	(")	36	17	27	15	8
Time & reappears	Average	(seconds)	128	128	128	131	100
	Range	(")	290-60	183-62	285-73	183-95	141-60
	No. entries	(")	34	16	25	13	7

REFERENCES

1. Meduna, L. J., and Gyarfas, K.: Motor and sensory phenomena during therapeutic carbon dioxide inhalation, *Dis. Nerv. Syst.*, 10:3, 1949.
2. Busse, E. W., and Parre, T. M.: Alterations of cerebral functioning produced by (a) diffusion respiration (b) prolonged carbon dioxide inhalation, *J. EEG Clin.-Neurophysiol.*, 2:231, 1950.
3. Goldenhohn, Eli S., Busse, E. W., Spenser, J. N., Draper, W. B., and Whitehead, R. W.: Studies of diffusion respiration VII the cortical electrical activity of dogs, *J. EEG Clin. Neurophysiol.*, 2: 33, 1950.
4. Engel, George L., Webb, J. P., and Ferris, E. B.: Quantitative electroencephalographic studies of anoxia in humans; comparison with alcoholic intoxication and hypoglycemia, *J. Clin. Invest.*, 24: 691, 1945.
5. Lyman, R. S., Carlson, W. A., and Benson, O. O.: Effects of reduced atmospheric pressure on the electroencephalogram, *J. Aviat. Med.*, 12:115, 1941.
6. Meduna, L. J.: Alterations of neurotic patterns by use of carbon dioxide inhalation, *J. New. Ment. Dis.*, 108:373, 1949.

Sodium Succinate Therapy in Multiple Sclerosis and Other Neurological Disorders

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The effects of sodium succinate therapy were observed in 65 cases including 51 cases of multiple sclerosis, six cases of amyotrophic lateral sclerosis, seven of Friedreich's ataxia, and one case of early Huntington's Chorea. These observations have extended over a two year period.

The salt of succinic acid was chosen because of its theoretical influence as a catalyst in the Krebs cycle of carbohydrates[1] and of fatty acid metabolism,[2] because of its value in the oxidation reduction of cytochrome and its influence preventing the inactivation of succinic dehydrogenase by oxidating glutathione, malonate, and such inhibitors that react with a sulfhydryl group of the enzyme[3,4,5] and also because of its function in the formation of acetyl choline.[6] Work by Aird[7] showed sufficient promise to motivate this investigation. The value of histamine therapy as well as of B_{12} (high and low potency) and of nicotinic acid are under comparative consideration.

Originally our patients were given sodium succinate by an initial intravenous injection of 20 c.c. of a 30 per cent solution. A gauge 25 caliber needle was utilized to insure adequate control. After the first two c.c. were administered, a dry sensation was felt in the throat. The patients responded to this dry sensation by attempts to clear the throat or by coughing, which raised at once the possibility that laryngeal vasodilatation might have played a part. After a minute or so, the effect of dryness faded, and the injection was continued at the rate of one c.c. per minute with a gradual tapering of the i.v. rate after 15 c.c. had been administered. At this time a flush became apparent over the face, neck and palms of the hands. Accompanying this flush was an intense feeling of warmth, generally over the entire body but most marked in the flushed areas. Neurological inventories before the injection were compared with any changes that resulted in an ensuing two hour period. Since our long-term results did not differ noticeably in those patients who had received an initial intravenous test with patients who were started at the outset wih oral dosages, the intravenous pilot injections were later abandoned as unnecessary. Oral administration was given by two level teaspoons (approximately 10 grams) three times daily, fifteen minutes before each meal; the sodium succinate crystals were dissolved in three to five ounces of water and followed by fruit juice, to counteract the salty taste. Patients who could not tolerate this taste, utilized rather large gelatin capsules filled with the above measured amount. Therapy was continued as long as evidence of improvement persisted and until such time as a withdrawal of medication did not result in an aggravation of the symptoms. Patients were re-examined as outpatients following discharge from the hospital at weekly intervals at first, and thereafter every two to three months.

Results:

A total of 51 cases of multiple sclerosis were given sodium succinate therapy. Of these, 23 revealed some slight initial changes in the neurological status, 18 revealed moderate changes and six revealed no alteration. Only one case presented exaggerated symptoms. Three cases were terminated because of side effects (such as gastrointestinal disturbance, diarrhea, constipation, nausea).

After six months of therapy, 37 cases studied revealed progression in three, a stationary course in two; 12 slight improvement; 17 moderate improvement; and three cases definite remissions.

At the end of a year, of cases followed, two showed progression; one death (see Case 1) had occurred after an initial improvement; one case remained stationary; three terminated therapy because of side effects; nine showed slight improvement; ten moderate improvement; four marked improvement.

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Case 1. V.K. (272552). A female patient, age 16, a sophomore in high school was admitted on 8-29-50 with complaints of nervousness and dizziness. In June 1949, she had fallen from a truck striking the occipital skull. No unconsciousness, but an immediate sensation, as though "marbles were rolling around in my head." She was "tense and irritable" for three days, developed emesis, nausea, and was hospitalized in her hometown for one week and a tonsillectomy was performed. Since then, she complained of a "funny feeling" in her head, of diplopia, and of headaches over the right temporal skull. Two weeks prior to admission, she had one fainting spell, apparent personality changes and lost her temper often. Review of her history was otherwise not unusual except for an appendectomy in 1948. Family history was non-contributory; she was the fifth of nine siblings, and had been a nervous youngster and had lost interest in school work and associations.

Physical examination: Bitten fingernails; blood pressure 140/100, mitral systolic murmur; pulse 88-96. Psychiatric status not unusual. Pupils equal with normal reactions; nystagmus on lateral gaze; discs and visual fields normal. Hearing unimpaired. The patient did not move the right arm as freely as the left, suggestion of rebound phenomena, left more than right. Muscle strength and coordination normal. Reflexes hypoactive and equal in the upper, but hyperactive in the lower extremities. Abdominal reflexes absent; bilateral strong flexor plantar responses. Synergic and equilibratory tests well executed. EEG: high voltage, 3-5/sec. waves in all leads, especially over the occipital region. Phenomoencephalogram: (9-12-15) minimal enlargement of the subarachnoid spaces over the parietal areas only. Spinal fluid formula revealed a 4433210000 gold sol curve. She was discharged without any therapy since symptoms and complaints had gradually subsided, but she remained under observation.

Six weeks before second admission, 8-25-51, diplopia had returned and a transient internal squint on the left was present which shifted to the right eye. She became ataxic and could not walk without assistance. There was weakness of the right arm with a "funny" feeling over the entire left face; several episodes of projectile emesis without clinical signs of increased intracranial pressure.

Examination (second admission): Paresis of the left external rectus with marked dissociation of bilateral eye movements presenting a rotary nystagmus. Bilateral temporal pallor (o.s. more than o.d.); visual fields normal. Hypesthesia to pin prick over the left face, the corneal reflexes bilaterally absent, left peripheral facial paresis. Hearing normal. Gait and all equilibratory tests markedly impaired by a cerebellar type of ataxia with abnormal posturing. Bilateral hypotonia and hyporeflexia with bilateral Babinski signs. Abdominal reflexes absent. No sensory disturbance except for left face. EEG: showed moderate 3-5/sec. waves in all leads, especially in the occipital region. On 9-11-51 the patient was placed on the regimen for sodium succinate. Immediately following the intravenous injections, she had the feeling of increased strength in the legs and was able to walk without as much ataxia as previously. There was less drift of the outstretched arms, finger-to-nose was improved bilaterally with only residual intension tremor, but no past pointing on the right; rebound phenomena continued. Increased strength in the right lower extremity; diplopia persisted with absent corneal reflexes. She was placed on oral sodium succinate and discharged. Upon returning after three weeks, she stated that she no longer had the "numb sensations" in the right arm and hand, although now there had been subjective numbness in the left leg. The left external rectus was of almost normal strength. Rotary nystagmus unchanged. Reflexes unaltered. Prior to her third admission on 12-30-51, the patient had reduced her succinate to 1 dram t.i.d.

Examination (third admission): Bilateral temporal pallor with perivenous sheathing; nystagmus on lateral gaze only; diplopia was almost absent. The uvula deviates to the right. Corneal reflexes were present; no impairment of the facial dysesthesia or hypesthesia. Generalized hypotonia in the upper extremity with cerebellar rebound marked intention tremor on finger-to-nose, distinct tremor of the head. Reflexes unchanged. The patient was placed again on full sodium succinate therapy. For the next three to four days she again showed improvement with reduction in ataxia and was able to walk without assistance. Dysarthria improved to test phrases; she was able to write legibly. At this stage the patient was placed on i.v. histamine therapy with oral sodium succinate without improvement, but with an increase in cerebellar dysfunction. After 25 daily infusions of histamine (½—2.75 milligrams), the patient was discharged on sodium succinate therapy. On 3-17-52 the patient stated that she had stopped sodium succinate for several weeks because of severe "flu" which, due to continuous emesis, prevented her from taking anything by mouth. Walking and persistent double vision were getting considerably worse despite the resumption of medication. Cranial nerves were as before with left abducens paresis. Cerebellar ataxia persisted with bilateral intention tremors and rebounding. Reflexes unchanged. Gait was markedly ataxic even in a walker. The patient's course at home since 4-1-52 was progressive with fever, increased tremors, and emesis. Death occurred on June 4, 1952. Post mortem could not be obtained and the clinical diagnosis remains speculative. Tumor cerebelli is unlikely; cerebellar hemorrhage is rejected with episodal improvement; olive-pointine cerebellar syndrome is most unlikely. We assume a demyelinating confluens process in the brain stem.

After one and one-half years, 15 cases revealed the following: Progression in two; no change in one; three more had terminated therapy; four showed slight improvement;

four moderate and one marked improvement. After two years one patient studied this long, remained improved. One case of multiple sclerosis with concomitant diabetes mellitus showed no intolerance to the drug, so far as his diabetes was concerned, but showed progression of the multiple sclerosis syndrome.

Case 2. E.Z. (279066). A male patient, age 35, had in 1941 transient episodes of diplopia associated with an attack of "flu." Diplopia recurred transiently in 1943. Admission on 9-28-51 because of recurrences of diplopia associated with left hemiparesis, blurring of vision, dysarthria, numbness in the legs, and urinary frequency. Neurological findings: Bilateral optic pallor, right more left; nystagmus, more on left than right lateral gaze; right facial asymmetry, slight weakness of the left grasp, dysdiadokokinesis on the left associated with mild weakness of the left lower extremity, especially in the flexor groups of the hip. Reflexes equal and active in the upper, hyperactive in the lower extremities with bilateral Babinski signs. Abdominal and cremasteric reflexes absent except for a right upper abdominal response. Lumbar puncture: gold sol 3333210000, but negative otherwise. The patient received 20 c.c. of 30% solution sodium succinate, which produced a mild flush but no objective evidence of improvement. He was placed next on oral dosage. When re-examined after one month, he no longer had double vision, he was able to walk for ten city blocks as compared to only several previously. His sense of balance had improved, and he "no longer walked like a drunk." The numbness of the lower legs had been greatly reduced.

Neurological examination: No nystagmus; slight tendency toward slurring; no intention tremor nor rebound phenomena; slight paresis of the left hip flexors as compared to more pronounced weakness on admission. Heel-to-knee function greatly improved. Babinski signs absent on the right. Abdominals and cremasterics remained bilaterally absent. On 11-20-51 numbness in the lower extremities absent; urinary frequency reduced from hourly to now normal urgency. No demonstrable weakness in the extremities; Babinski sign absent bilaterally. In 1-11-52 the patient had reduced his sodium succinate to one dram t.i.d. and was continuing to improve in strength, encountering very little difficulties with equilibratory functions. Neurological inventory was normal aside from absence of abdominal and cremasteric reflexes and the bilateral optic temporal pallor. On 3-10-52 he reported a transient episode of dysarthria which had cleared up after several weeks; that for thre days during damp, muggy weather he had experienced a return of the leg ataxia. Examination revealed a questionable plantar response on the right, but abdominal reflexes had returned in the upper quadrants. When seen on 5-12-52 only bilateral Babinski signs present. On 9-12-52 the patient showed return of abdominal and cremasteric reflexes with a questionable right plantar response only. All coordination tests well performed. The patient had been able to go hunting in the Fall, as he had before his illness; he still did not feel well enough to resume his work as a pipe fitter. The neurological inventory was essentially normal, except for absence of abdominal and cremasteric reflexes; no visual complaints. On 1-10-53 neurological inventory was normal except for absent abdominal and mremasteric reflexes. Examination on 5-21-53 no progression, no physical difficulties. Patient is under continuous therapy with succinate.

Case 3. A.T. (279236). A 28 year old white female was admitted to the hospital on 10-9-51. About June of 1951 she had experienced numbness behind the left ear followed by numbness in both feet with a sensation of constriction around the chest; listlessness, lack of coordination of both arms, unsteady gait. These complaints cleared up only to return four months later. With the second exacerbation she developed headache, nausea and vomiting necessitating admission. She was lethargic, apathetic, and acutely ill with nausea (temperature 98°, pulse 82, blood pressure 115/80) and frequent gagging. The left pupil was larger than the right; the left eye could not follow objects on the left lateral gaze. A small hemorrhage inferior to the left disc was present. There was marked peripheral paresis of the left face without absence of taste on the left anterior 2/3 of the tongue. Severe ataxia of the left extremities, hyperreflexia with clonus of the right patella and a positive left Babinski. Hypesthesia of the left face and left cornea. No contributory physical findings; no allergies. On one occasion the patient had a right sided tonic seizure involving the right arm and right face not accompanied by loss of consciousness. The neurological signs shifted from day to day with increased involvement pointing to the brain stem. Lumbar puncture: normal pressure, color, and laboratory findings. Pneumoencephalogram: (10-26-52) some enlargement of the subarachnoid spaces, but no space filling lesion. The patient was given sodium succinate initially by the intravenous regimen. Subjectively the patient felt less "sick and dizzy" but was without objective evidence of neurological improvement after several hours. Three days later some decrease in the paresis of the left sixth and seventh nerves. The left facial hypesthesia had disappeared, and the corneal reflex was normal. Tongue deviated slightly to the left. There were slight intention tremors.

On 11-15-1951 return of function of the extraocular muscles was obvious, the patient was able to walk with the walker or by holding on. By 11-26-51 she was walking with some assistance, but was still very ataxic. Her vision had improved in the left eye. By 12-2-51 her vision had continued to improve, and she was without diplopia. Following her discharge on 12-15-51, the patient was seen ambulatory. By February 1952 the patient's balance had improved to the extent that she could walk

up and down stairs; she was doing all her housework, and she was able to carry and to care for her 18 months old youngster alone. She had slight difficulty in utilizing her right hand, which felt clumsy and numb. There remained residual numbness of the left face, less than formerly. Nystagmus on vertical and horizontal gaze, but no diplopia. Corneal reflex now active on the left. The left pupil was still larger than the right. Slight dysarthria. Romberg was negative. Gait revealed a widened base with minimal ataxia. On 4-9-52 the patient started to lift her legs up in walking. She stated that she had omitted the sodium succinate for one week, and during this interim had felt extremely fatigued and that her eyes focused poorly. Upon resumption of the drug, she regained her strength, vision and balance. She still had occasional feelings of numbness over the left tongue and face, could do all her housework and cared for their three children.

Examination: suggestion of hyperesthesia over the left face, slight dysarthria, reflexes as before. The patient was seen on 9-16-52, 11-17-52, and 1-5-53. The neurological picture remained fairly constant with increased feeling of well being which was not attributable to euphoria. On 11-17-52 she reported that she had reduced her succinate to 1 dram and after several days had begun to stumble again. On 3-17-53 the patient revealed an increase in all cerebellar phenomena with a left Bell's palsy. Sodium succinate dosage was increased to 2 drams t.i.d. When reexamined in May 1953, all symptoms had completely disappeared. The patient remains on maintenance dosage of sodium succinate.

Six cases of amyotrophic lateral sclerosis: none of them revealed any beneficial response to sodium succinate therapy.

Seven cases of Friedreich's ataxia: one case had a slight improvement but the results were equivocally different in the remainder.

The case of early Huntington's Chorea revealed improvement over a period of seven months of continued administration, manifested by reduction in the severity of the choreic movements and a marked improved mental status.

Patients with multiple sclerosis reported improvement in strength, in well being, in mental alertness, and in their coordinated efforts. In some cases the therapy was continued because of an improved subjective feeling of well being which, however, was not measurable objectively. Patients with paralyses in flexion and strong withdrawal phenomena as seen in complete cord lesions, did not experience amelioration, though they testified often to a reduction in the painful muscle spasms. In several cases corticospinal tract symptoms were completely abolished and the Babinski phenomenon could not be evoked.

Discussion

Physicians, especially neurologists, are often accused of not treating chronic neurological disease, but merely recording, like historians, the progressive march of a disease process. This has been particularly true in multiple sclerosis with its notorious remissions and exacerbations which have taken place irregardless of any therapy schedules. A claim to having benefited the course of this condition may bridge on opportunism. For this reason we have followed our patients for long periods of time up to two years. We have seen therapeutic promises turned into failure by the passage of time, though others have shown an arrest or an improved clinical picture.

We, therefore, deal with impressions only which would lead to the following conclusions: Sodium succinate is not a panacea; it produces changes shortly after initiation of therapy, evident both objectively and subjectively. Progression can and does occur in some cases even during optimal and prolonged therapy with sodium succinate. Side reactions are no more frequent than with other forms of treatment. Sodium succinate is, by and large, equivalent to histamine treatment alone. The degree of improvement noted after onset of sodium succinate therapy does not necessarily indicate the maximum level of response which might be anticipated with continued use of the durg. Withdrawal of medication will sometimes result in exacerbation of symptoms. Sodium succinate is a safe medication even in the presence of hypertension and diabetes mellitus.

The exact mode by which sodium succinate exerts its influence is not known. The work of Lumsden[8] suggests that the oligodendrocytes might dissappear very early in the involved regions of the central nervous system. The oligodendroglia cells are said to be necessary for the maintenance of lipid metabolism of the myelin sheaths. The absence of "these key cells" to carry on the metabolism of the myelin sheaths may be a crucial factor in the production of demyelinating symptomatology. Perhaps by sup-

plying predigested metabolites, sodium succinate as such is able to bring about the improvement in metabolism of the affected areas. Its catalytic effect might also be mirrored in improved general metabolism in the non-involved areas of the nervous system.

Another suggestion is that the benefit of sodium succinate is dependent on its alkalinizing effect alone and not on its enzymatic properties. The relatively small amounts utilizing in terms of the body's metabolic requirements favor such a postulate. However, such influence cannot be demonstrated symptomatically by tetanic or laboratory phenomena, although several patients were unable to tolerate sodium succinate because of vertigo, giddiness or gastrointestinal cramp-like sensations.

The element of suggestion cannot be denied. The patients became aware of the fact that a new substance or drug was being utilized. One patient failed to continue the medication on the assumption that it was actually a form of "saltpeter designed to reduce his libido." On reassurance, he experienced clinical improvement with resumption of the drug that he had not noticed previously.

Further investigatory efforts are being pursued to determine whether such factors as the antagonists of succinic dehydrogenase may be modified so as to enhance the effectiveness of this medication. Calcium salts plus vitamin D were added to the sodium succinate therapy in light of this theory[5,9] with slightly improved responses in four of eight patients who were given this adjuvant therapy. Were a living culture of oligodendroglia possible as by the method outlined by Lumsden,[8] the direct effect of the drug on these cells could be studied in vitro. In several cases, combined sodium succinate and histamine therapy were given, but these patients showed no greater improvement over that which was obtained with succinate alone. Some patients developed a delayed intolerance to the drug after months, and in one instance, after one year. Ten cases continued to show progression after initial period of improvement. Short episodic exacerbations of new symptoms occurred in several cases while under therapy, but these cleared up and perhaps the exacerbations were not of the same duration that might otherwise have occurred. One case, already mentioned, after a rapidly progressive course of eight months' illness, during which she had seemed to respond to the drug, finally died in the eighth month of therapy (no autopsy could be obtained).

Summary

Sodium succinate was given to 65 patients, including 51 cases of multiple sclerosis. Favorable influences upon the progress of the illness were observed in some of the cases of multiple sclerosis. A discussion of the mode of action, as well as the implications for further study to determine more about the mode of action and factors that may influence the supposed substrate activity of this substance is given.

BIBLIOGRAPHY

1. Krebs, H. A.: Intermediary stages in biological oxidation of carbohydrates. *Advances in Enzymology*, 3:191, 1943.
2. Potter, V. R., and Albaum, H. G.: Studies on mechanism of hydrogen transport in animal tissues; inhibition by ribonuclease. *J. Gen. Physiol.*, 26:443, 1943.
3. Hopkins, F. D., and Morgan, E. J.: The influence of thiol groups in the activity of dehydrogenases. *Biochem. J.*, 32:611, 1938.
4. Hopkins, F. D., Morgan, E. J., and Lutwab-Mann, C.: The influence of thiol groups in the activity of dehydrogenases. Journal? II, 32:1829, 1938.
5. Axelrod, A. E., Sevingle, K. F., and Elvehjem, C. A.: The stimulatory effect of calcium upon succinoxidase activity of frseh rat tissues. *J. Biol. Chem.*, 140:931, 1941.
6. Torda, C., and Wolff, H. G.: Effect of malonate, fumarate, succinate, and citrate on synthesis of acetyl choline in vitro. *Proc. Soc. Exper. Biol. and Med.*, 57:234, 1944.
7. Aird, R. B.: Succinate therapy in multiple sclerosis. *Neurology*, Vol. 1, No. 3, May-June, 1951.
8. Lumsden, C. E.: Fundamental problems in the pathology of multiple sclerosis and allied demyelinating diseases. *British Medical J.*, May 12, 1951.
9. Walker, B. S., Boyd, W. C., and Asimov, I., "Biochemistry and Human Metabolism," p. 224, *The William & Wilkins Co.*, Baltimore, 1952.

of the drug that he had not noticed previ-

Authors' Note: Since submitting this report two additional patients have died. One, the spastic paraplegic with severe head tremors, died of pneumonia following an appendectomy. The other, the familial multiple sclerosis case with severe diabetes millitus, died suddenly after a progressively downhill course. In neither case was a post mortem obtained since both patients died in out of town hospitals.

Effect of L(+) Glutamic Acid on Physical Growth and Development

(A Study of 101 Cases)

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Glutamic acid has been used experimentally in the treatment of mental deficiency since the report of Price, Waelsch and Putnam in 1943. Although large amounts of this material have been fed to patients, there have been no systematic studies of its effect upon growth and development when used over long periods of time. A project for the study of the effect of glutamic acid on mental growth initiated in the Child Welfare Clinic of Children's Hospital, Washington, D.C., in 1946 afforded an opportunity for a long range series of observations.

Mild symptoms of toxicity were reported by Zimmermann.[3] The authors investigated the possibility that prolonged feeding of glutamic acid, which plays such a significant role in metabolism, might have subtle and even harmful effects on physiologic functions, detectable as alterations in growth trends, body chemistry, or the hematologic picture. On the other hand it seemed equally possible that the reported favorable effects on mental growth might be due to an improvement in physical status.

Procedure of Study:

Detailed family, prenatal, birth and postnatal histories were taken by a pediatrician. Complete physical examination, including neurologic and endocrinologic consultations, were performed on each child. X-ray films were made of the carpal bones to check skeletal maturation. A complete blood count, Kahn and Mazzini tests, blood cholesterol determination, liver function tests, and urinalysis, including a test for the presence of phenylpyruvic acid were included in the preliminary study. Cephalin flocculation tests were used as liver function tests at first, but were replaced during the second year by thymol turbidity tests. When indicated, additional data were obtained through eye consultations, audiometer tests and encephalograms. The clinic secretary contacted the parents or guardians every month for a report of changes noted by them, difficulties in giving L(+) glutamic acid and other pertinent problems. Physical examinations and neurologic consultations and laboratory tests were repeated every six months. Endocrinologic consultations were repeated only in indicated cases. Wetzel grids were kept on all patients except a few for whom data could not be plotted on either the infant or childhood grids.

Congenital Stigmata:

There was a high percentage of congenital stigmata present in these children (66.3%). Although we realize this has no direct bearing on the effect of glutamic acid on physical growth, it is of value in helping the reader to understand better the type of child with whom we were working.

The congenital stigmata were classified as follows:

Pronated feet	31
Eye conditions	26
Strabismus	22
Microphthalmia	1
Cataract	1
Nystagmus	1
Myopia	1
Congenital heart disease	5
Hernia	4
Deformity of fingers or toes	4
Malocclusion	2
Deafness	2
Birth mark	1
Genu valgus	1
Cloacal anlage	1
Harelip	1
Undescended testicles	1

Of these 101 children, ranging in age from two weeks to thirteen years three months, the length of time of administration of L(+) glutamic acid was as follows:

35 children	6 months
29 children	12 months
21 children	18 months
16 children	24 months

History—prenatal, birth, and postnatal:

There were positive family histories (mental retardation, epilepsy or neuropsychoses) in 24 instances (24.2%), positive pregnancy factors (multiple pregnancy, toxic symptoms, illness or accidents during pregnancy, Rh negative blood of mother, or threatened abortion) in 45 instances (45.4%), and birth factors (prematurity, difficult delivery or anoxia) in 31 instances (31.3%).

Physical Examinations:

The general appearance and state of nutrition were classified as good (G), satisfactory (S), and poor (P) regardless of the presence or absence of acute infection such as nasopharyngitis or otitis media. On this basis no child regressed during his period of observation and 29.7 per cent showed improvement.

For more objective evaluation, the Wetzel grids were employed. Individual heights, weights, and ages of these children as measured at each physical examination at six month intervals throughout the study were plotted on the grids, and all measurements obtained from previous hospital records, schools, clinics, and family physicians were plotted for the time prior to this study. Because 16 individuals fell in the group between the infant and childhood grids, only 85 children could be included in this portion of the study—23 on the infant grids and 62 on the childhood grids.

These children were divided into two groups. The first group was composed of those on whom previous height and weight determinations were available so that their growth and development prior to our study could be plotted. The second group included those children on whom no previous records could be obtained.

There were ten infants and 28 children in the first group. The results in channel trends of the 28 patients plotted on the Wetzel grids for children are shown in Table 1.

TABLE 1

Age	Upward (toward more obese A4 Channel)	No Change	Down (toward poor B4 Channel)
½-1 yr.	(1) 33.3%	(2) 66.6%	
1-2 yrs.	(2) 28.5%	(3) 42.8%	(2) 28.5%
2-5 yrs.	(2) 50.0%		(2) 50.0%
5-8 yrs.	(4) 26.7%	(6) 40.0%	(5) 33.3%
8+ yrs.	(2) 21.1%	(6) 66.6%	(1) 11.1%
Totals	(11) 29.0%	(17) 43.7%	(10) 26.3%

These same children were divided into three groups labelled Stocky, Medium, and Slender, according to their position on the Wetzel grid channels. The following chart demonstrates the changes in body builds which occurred between the examination prior to the use of glutamic acid and that made at the termination of the course of glutamic acid.

TABLE 2

	Stocky	Medium	Slender	Totals	No.
More Stocky		41.1%	25.0%	28.5%	8
No Change	57.1%	41.1%	25.0%	42.8%	12
More Slender	42.8%	17.6%	50.0%	28.5%	8

For the children in Group I maturation was determined just prior to the use of glutamic acid and again at the culmination of the course of glutamic acid.

TABLE 3

Age	Prior to G.A.			After G.A.		
	A	N	R	A	N	R
½-1 yr.	2		1	2	1	
1-2 yrs.	2	2	3	1	3	3
2-5 yrs.	4			3	1	
5-8 yrs.	7	3	5	8	2	5
8+ yrs.	3	2	4	4	1	4
Totals	18	7	13	18	8	12
%	47.3	18.4	34.2	47.3	21.0	31.6

"A" indicates the child was advanced above the 67% line or standard development.

"N" indicates the child followed the normal auxodrome of its age.

"R" indicates the child was retarded behind the 67% line or standard development.

Group II comprised 47 children on whom no height and weight determinations had been made prior to our study. For this group maturation attained prior to the use of glutamic acid was compared with that at the termination of a course of glutamic acid.

TABLE 4

	Prior to G.A.	After Course of G.A.
Totals:	73.5% A	76.4% A
	8.8% N	5.8% N
	17.6% R	17.6% R

See explanation on Table 3.

In an attempt to correlate the size of the average dose of L(+) glutamic acid received by each individual with any change in physical growth and development the following chart was developed using maturation as the means of comparison. The letters "A," "N," and "R" have the same meaning as in pre-

vious charts. The dosage is measured in Grams/10 pounds of body weight/day.

TABLE 5

Dosage	0-2.0			2.1-4.0			4.1-6.0			6.1+		
	A	N	R	A	N	R	A	N	R	A	N	R
Children:												
Before G.A.	11	3	4	21	4	9	3	1		4		2
After G.A.	12	2	4	22	3	9	4	1		3	1	2
Infants:												
Before G.A.	4	1	1	1	3	2	2	1	4			4
After G.A.	2	3	1	2	2	2	2	1	4	1	1	2
Totals:												
Before G.A.	15	4	5	22	7	11	5	2	4	4		6
After G.A.	14	5	5	24	5	11	6	1	4	4	2	4

The data in these charts indicates that children receiving large doses of glutamic acid were not affected differently from those receiving smaller doses.

Laboratory Data

Blood counts were done every six months. The results of the initial and final counts were compared in order to determine the effect of L(+) glutamic acid on the hematopoietic system.

Summary of Laboratory Data

	0	—	+	
	No Change	Decrease	Increase	Not Done
RBC	46	18	23	14
Hemoglobin	42	17	28	14
WBC	63	9	14	15
Thymol T.	83		3	15

Red blood cells were considered to have increased (+) if they showed an increase of 500,000 cells/mm^3 or more, and decreased (—) if they decreased 500,000 cells/mm^3 or more. There was no change in the red cell count in 52.9 per cent of the children, while according to our criteria 20.7 per cent decreased and 26.4 per cent increased. The mean initial red blood cell count was 4,060,000; after receiving 1+ glutamic acid it was 4,080,000.

Changes in the number of grams of hemoglobin per cu. mm. were considered to be significant if there was a deviation of 1 gm more or less from the original hemoglobin level. There was no change in 48.3 per cent of the children. The hemoglobin decreased in 19.5 per cent of the children and increased in 32.2 per cent. The average initial hemoglobin estimation was 12.39 gms; after receiving L(+) glutamic acid it was 12.62 gms.

Iron was presscribed in addition to the L(+) glutamic acid in seven cases because of hypochromic anaemia. Three of these children showed an increase in hemoglobin, three showed no improvement, and one had a decrease in hemoglobin.

For white cells, a range of 5,000 WBC per cu. m.m. to 10,000 WBC per cu. m.m. was considered to be normal. The white blood cell count stayed within normal limits in 62.7 per cent, was unchanged in 73.1 per cent, decreased below normal range in 3.5 per cent, and increased above normal range in 4.7 per cent. The average initial white blood cell count was 7,708 WBC; after receiving 1+ glutamic acid it was 7,780 WBC.

All urinalyses were within normal limits except in two cases (siblings) in which tests showed the presence of phenylpyruvic acid.

Cephalin flocculation tests and thymol turbidity tests were done to detect the presence of liver damage. All initial tests were within normal limits. One child had a positive cephalin flocculation test and three children had thymol turbidity tests of six or above (although only one was over ten, which is considered by some workers to be the upper limit of normal). The thymol turbidity test was normal in the one child with a positive cephalin flocculation test. One of the children with an abnormally high thymol turbidity test gave a normal cephalin flocculation test. The other two abnormally high thymol turbidity tests were not checked with cephalin flocculation tests.

The effect of L(+) glutamic acid on certain clinical types of mental retardation:

Mongolism: These children offered an especially interesting group to observe because of their altered rate of growth. There were 11 Mongoloid idiots in our study, ranging in age from two weeks to 12 years. When their heights and weights were plotted on Wetzel grids, three children gained in physique channels, two lost in physique channels and six stayed in the same channel. On Wetzel's maturation chart five showed gains in their development levels, four showed losses in developmental levels, and two stayed at the same developmental level.

Hypothyroidism: Four mentally retarded children suffering from hypothyroidism are

included in our group. Their ages varied from four to 11 years. Prior to this experiment, each had been treated with thyroid extract in adequate amounts resulting in satisfactory physical growth. During the experiment the administration of thyroid extract was continued in a routine manner. On Wetzel grids two children showed a loss of one or more physique channels and two children showed a gain in physique channels. On the maturation chart three children showed a gain in developmental level. At the close of the study two children were in the retarded group and two children were in the advanced group of developmental levels.

Toxic Symptoms: Toxic symptoms due to L(+) glutamic acid occurred in 24.8 per cent of the cases. These were determined by a careful review of the notes made of the parents' monthly reports and clinic visits. No symptoms were noted as being present unless they occurred constantly during the period the child received L(+) glutamic acid. In many instances they would disappear after maintaining the same dose over a period of time. None of the symptoms were of a serious nature nor did they have a harmful effect. As noted above, L(+) glutamic acid causes no deleterious effect on the liver, kidneys or hematopoietic system. The most common symptoms were nausea and vomiting which occurred fairly constantly in 13 patients. In many instances the children disliked L(+) glutamic acid intensely because of its taste and consistency, in spite of ingenious methods employed by the mother to disguise the unpleasant qualities of the medication. These 13 instances of nausea and vomiting, however, seemed to result from a toxic effect of the drug rather than a psychological reaction to it. This agrees with evidence that glutamic acid administered intravenously causes nausea and vomiting. In three children who had atopic eczema, an increase in intensity of the rash could be correlated with the increase of dosage of L(+) glutamic acid. Nocturia and frequency occurred in two patients. Two of the children were restless and hyper-irritable when receiving a relatively small dosage of L(+) glutamic acid. Diarrhea was present in two children. Single instances of headache, abdominal pain and diaper rash were reported.

Summary

The absence of changes in the physical status of children fed glutamic acid is worthy of comment. Some of these children were receiving over thirty percent of their nitrogen intake in the form of glutamic acid. This would represent an increase of over five fold in the normal glutamic acid content of the diet. Since this medication was usually taken with meals a highly unbalanced mixture of amino acids must have been absorbed. It appears that supplementation of the diet with non-essential amino acid has no effect at least so long as some essential amino acids are ingested, and so long as the total nitrogen requirement is completed with an easily utilized source of nitrogen, in this case glutamic acid.

Our results with Mongoloid children do not agree with those reported by Zimmermann[6] who noted physical gains when treating these children with glutamic acid. There is no explanation for this discrepancy. Our group of Mongoloid children was considerably smaller than his. The four hypothyroid children included in our study showed no consistent alteration in growth during the experimental period.

Conclusions

1. Administration of up to 1.75 grams of L(+) glutamic acid per kilogram of body weight per day to mentally deficient children has no effect upon the physical growth and development as measured with the Wetzel grid.

2. The medication has no effect upon the total or differential white blood count, the red blood count or hemoglobin, or the thymol turbidity test.

3. Glutamic acid, in dosage now being utilized in the experimental therapy of mental deficiency, has no discernible long range toxicity.

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BIBLIOGRAPHY

1. Price, J. C., Waelsch, H., and Putnam, T. J.: D1 Glutamic Acid Hydrochloride in Treatment of Petit Mal and Psychomotor Seizures, *J.A.M.A.*, 122:1153, 1943.
2. Zimmermann, F. T., and Ross, S.: Effect of Glutamic Acid and Other Amino Acids on Maze Learning in White Rate, *Arch. Neurol. and Psychiat.*, 51:446, 1944.
3. Zimmerman, F. T., Burgemeister, B. B., and Putnam, T. J.: Group Study of Effect of Glutamic Acid upon Mental Functioning in Children and Adolescents, *J. of Psychosomat. Med.*, 9:1175, 1947.
4. Zimmermann, F. T., Burgemeister, B. B., and Putnam, T. J.: Effects of Glutamic Acid on Mental Functioning in Children and in Adolescents, *Arch. Neurol. and Psychiat.*, 56:489, 1946.
5. Zimmermann, F. T., Burgemeister, B. B., and Putnam, T. J.: Ceiling Effect of Glutamic Acid upon Intelligence in Children and in Adolescents, *Am. J. Psychiat.*, 104:593, 1948.
6. Zimmermann, F. T., Burgemeister, B. B., and Putnam, T. J.: Effect of Glutamic Acid in Intelligence of Patients with Mongolism, *Arch. Neurol. and Psychiat.*, 61:275, 1949.
7. Zimmermann, F. T., Burgemeister, B. B.: Effect of Glutamic Acid on Mental and Physical Growth of Mongols, *Am. J. of Psychiat.*, 105:661, 1949.
8. Albert, K., Hoch, P., Waelsch, H.: Preliminary Report on Effect of Glutamic Acid Administration on Mentally Retarded Subjects, *J. Nerv. and Mental Dis.*, 104:263, 1946.
9. Kerr, W. J., Szurek, S. A.: Effect of Glutamic Acid on Mental Function: Pilot Study, *Pediatrics*, 5:645, 1950.

The Improbable and the Impossible

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> Man can believe the impossible, but man can never believe the improbable.
>
> *Oscar Wilde.*

The logical contradiction—belief in the impossible coupled with disbelief in the improbable—has long been noted, but no explanations have been forthcoming to account for the paradox. The paradox is merely restated in aphoristic terms, as, for example, in Montesquieu's allusion to pagan religions: "Man cannot make a worm, but makes gods by the dozen."

When the Frenchman, Leban, invented the gas lamp, nobody believed the "improbable" assertion that a lamp could burn without a wick. Leban's beloved Paris was not lit by gas until fourteen years after the inventor's death. When Edison demonstrated his first phonograph, a great French authority "exposed" the invention as "a typical American hoax," explaining that Edison had simply hired a ventriloquist. Nobody believed that the improbable, a "talking machine," could exist. The history of inventions is crowded with similar examples. The fact per se is known only too well.

On the other hand the history of superstitions proves exactly the opposite: the impossible is readily believed. It is quite conceivable that those who were skeptical of Leban's and Edison's inventions believed in —ghosts.

What is the meaning of this logically inexplicable dichotomy?

The riddle becomes less mysterious upon application of psychiatric experiences with the two systems: of consciousness and of the unconscious. *Conscious reasoning is used in judging the improbable; in "judging" the impossible, infantile megalomania and omnipotence emerge from the depths of the unconscious* and are applied to the problem. The two phenomena—the improbable and the impossible—are thus judged by *different yardsticks.*

The interconnections are even more complex. In insisting that the improbable is impossible, an unconscious mechanism enters the picture: repressed fear. Once-upon-a-baby-time, everything new was frightening. These massive infantile fears were partially exorcised, later on, by adaptation to reality; they were also partially repressed. When the individual is confronted with the unknown, these fears are unconsciously revived, to be counteracted with stubborn rejection: "I don't believe it."

Why does the same process *not* take place when the individual is confronted with the "impossible"? The probable answer is that the allure of infantile megalomania is too great to be passed over lightly. It is only in our conscious ego that we insist on logic, consistency, and congruity. Infantile "metalogic" works differently. Alluding to contradictions in dreams, Freud once adduced the old joke about a man who borrowed a pot from a neighbor, and returned it, broken. When the neighbor indignantly objected, the culprit defended himself: "First of all, I never borrowed a pot from you; second, I returned it in perfect condition; third, it was already broken when you gave it to me." Obviously, all three excuses cancel each other out, but not from the viewpoint of the infantile unconscious.

*

In the clinical treatment of neurotics, every psychiatrist who makes use of unconscious mechanisms is constantly faced with the patient's disbelief. The entire concept of the unconscious, and application of unconscious mechanisms, is declared "improbable," and is attacked with every weapon stored in the arsenal of logic and common sense. When the patient is informed that the unconscious utilizes a denomination other than logic, namely, repressed wishes, repressed guilt, repressed double defenses, he tends to flounder for a time, but soon reverts to his previous "common sense" argument.

Technically, this problem is solved in the analysis of transference and resistance: emotional repetitions which after a long period of time convince the patient—*emotionally*. The joker in the pack is that the absence of "logic" is one of the means through which the recalcitrant patient is convinced, for some of his reactions are so irrational that no logical explanation is possible. Then, the formula is suggested: *"Where logic ends, the unconscious takes over."*

A patient of mine, a shrewd and witty fellow, once slipped on a carpet in my waiting room, and immediately (half in irony) accused me of having placed this particular carpet in this particular way so that he would "break his neck." The half-joke, in inner reality, referred to something quite serious. In the transference repetition, he unconsciously projected upon me the image of the "bad, cruel mother," to whom he imputed all possible evil designs. After explaining this interconnection (which did not impress the patient at all), I added, replying in kind to his irony: "Imagine for a moment that your conclusion is correct: Think of the trouble I would be getting myself into—calling for an ambulance, having you transported to a hospital, visiting you at the hospital, notifying the insurance company, and so on. And—if you should really die—I would lose a good patient." This little scene was far more effective than a lengthy explanation in convincing the man of the reality of the unconscious.

The dichotomy of belief in the impossible and disbelief in the improbable is especially noticeable in patients who are profuse and eloquent in offering "proof" that the unconscious is "improbable," while at the same time they cherish some completely irrational convictions. One such man, a gambler, admitted with some reluctance that when he watched (on television) a race in which he had backed one of the entries, he would cross and recross his legs in a specific manner. These movements were secret signs directed at the jockey, whom he did not know personally, and who in any case could not see him. Here the belief in the impossible is clearly connected with infantile megalomania. One is reminded of the brilliant description of the four-year-old Jean Christophe in Romain Rolland's novel of the same name:

> He is also a magician. He wanders with great strides through the fields, gazes at the sky and gestures with his arms. He commands the clouds. He wants them to move to the right. But they move

to the left, and he scolds them, and repeats his command more vigorously. With beating heart he watches from the corner of his eye to see if at least one will not obey him. But they all sail quietly toward the left. Now he stamps with his foot and threatens them with a stick and calls to them to move to the left. And sure enough, this time they 'obey orders.' He is happy and proud of his power."

*

Inwardly, remnants of infantile megalomania are never fully relinquished; these remnants hide behind many masks. (This factor has been elaborated on in "The Basic Neurosis" and "The Superego," Grune & Stratton, 1949 and 1952.)

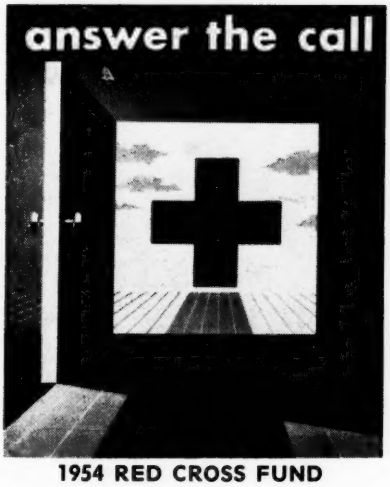
It is not easy to accept the fact that logic and common sense preside only over a restricted radius of the personality. A writer of distinction, in analysis because of writer's block, told me during the last stages of his cure:

"The most terrifying shock I experienced in analysis was the realization of something you explained to me in the beginning, unemotionally, and as a statement of fact. You said that when we are confronted with an unconscious conflict, our conscious thinking falls fully under the dominance of the unconscious, and that we are doubly deluding ourselves because we are misusing our logic to bolster our emotionalism. To tell you the truth, I considered your statement a rather silly sales talk at the time. Then I found out that you were understating the facts: our greatest intellectual achievement, the one we brag about, is the mind, and the mind does the bidding of the unconscious! What an ironic comment on our alleged achievements! To formulate it precisely, I would say that the mind is a prostitute who sells herself to the highest bidder. And in situations of conflict, the unconscious obviously has a bigger bankroll than our 'superior' consciousness. Our logic and common sense vanish, leaving a silly fool replete with self-deception. What an arrangement—worthy of idiots, not of the cultured being homo sapiens pretends to be! The mind is a prostitute, and that is our maximum achievement! Like that prostitute scribbler, the hack writer, who sells his pen or typewriter, we are all *hack thinkers*, and we don't even profit by it. Idiotic hack thinkers, that's what we are; homo sapiens—the hack thinker!"

The man who uttered these words, and coined the phrase, "hack thinker," was decidedly bitter about the predominance of the unconscious. The last phase of his treatment was devoted to reconciling him with Faust's "You believe you impel, and are impelled yourself." Even then, he had to part with infantile megalomania.

Subtracting the emotionalism involved, the patient was on the right track. The target of his indignant complaints is one of the elementary axioms of dynamic psychiatry: the unconscious is more powerful than is consciousness. Consciousness, we know, is really great only in self-deception.

251 CENTRAL PARK WEST



1954 RED CROSS FUND

Development of a True Paranoia

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The question of the paranoid illnesses has been characterized in a standard psychiatric text as one of the most difficult in the field.[1] In particular there is still sharp division of opinion both in theory and practice as to the existence and relationships of the cluster of symptoms called pure paranoia.[2] Kraepelin attributed the defective knowledge and great differences of viewpoint in this domain to the difficulty of accumulating cases and ascertaining facts about them.[3] The number of well-documented cases of pure paranoia is still small. This statement can be readily confirmed by a perusal of American, British and German texts on psychiatry or abnormal psychology, which show a marked tendency to copy illustrative cases of the disorder from one to another. The history of the following patient appears to deserve record as an addition to the treasury of cases on which the definitive theory of paranoia will eventually rest. The case was unanimously diagnosed by several independent psychiatrists as true paranoia and its development is now known in full detail.

Mr. S., the patient, had no family history of behavioral disorders. His early life imposed unusual stresses but he reacted favorably. His father was a clerk and he was the second of five children. When S. was six his father died of pneumonia, with the result that the financial circumstances of the family became very difficult. The mother was an inflexible member of a strict religious sect. The concepts of sin and duty to God acquired vital importance for S. At the age of nine he was admitted to an orphan school. He was well content there and he was also well content on his regular visits home. Throughout his childhood and adolescence no psychoneurotic traits or other evidences of maladjustment were ever observed by relatives or teachers.

It was early realized that S. was exceptionally intelligent. He was also exceptionally hard-working and at sixteen obtained a scholarship from the orphan school to a nearby university. He studied mathematics, took a first-class degree and won another scholarship to a university of higher status. At the latter he attained the greatest distinction possible for a student of mathematics in England.

From Research Department, Netherne Hospital.

By that time the First World War was well under way and he joined the Navy as an officer-instructor in mathematics. His life in the Navy was uneventful and without special stress. He was not regarded as in any way abnormal either at the two universities or in the Navy.

After the war S. joined the administrative Civil Service, a career frequently chosen in England by graduates of high ability. He established a home for his mother and an unmarried sister near his work. In order to provide for their maintenance he decided that he would remain a bachelor. He devoted most of his spare time to study, though he still played certain games, especially lacrosse. He took a degree in law and was called to the Bar. Subsequently he took a degree in economics. His intellectual ability and industry greatly impressed his superiors in the Civil Service. His advancement in salary and status was not, however, commensurate with his capacity. Promotion was slow for everyone at that time. S. gave no overt expression to frustration at this but by the age of 30 he was regarded as a person difficult to handle and inclined to resent criticism or control. These traits were not sufficiently pronounced to hinder his promotion to a higher grade at the age of 38. No one at this period regarded him as an individual outside the limits of normal adjustment.

From the age of 42 onwards S. conducted a series of exposés of small-scale wrongs, neglects and inefficiencies in his department. Most were exceedingly trivial. Some were without foundation, others were based on real wrongs. Of course, these activities did not endear him to his superiors. He was still exceptionally studious but his attachment to the strict religious sect had become looser. After the death of his mother, when he was 47, he broke off all contact with other members of his family except for the unmarried sister living with him. He had no friends with whom he discussed his reading and ideas. At the age of 48 he was passed over for promotion. His superiors thought it plain that his peculiarities unfitted him for a position of great responsibility. By this stage there is little doubt that he would have been diagnosed as a paranoid personality.

Shortly after his failure to gain promotion S. unearthed a genuine, though relatively minor, malpractice in his department. The matter was with difficulty suppressed and he was transferred to another department. Here he devoted all his spare time to reading the historical and legal background of his new work. He made himself master of ancient and recent correspondence in the filing system. It was not long before he discovered a far more important wrong than any of the earlier ones.

A certain commodity had formerly been taxed both when used as a luxury and when used for industrial purposes. Those who employed it industrially, however, received a rebate on the tax paid. The tax on the industrial use of this commodity had long since been removed but the rebate still continued to be paid by the government. This hidden subsidy cost the tax payers a million pounds a year.

S. drew the attention of his immediate superiors to these facts but he was brushed aside. He went to more remote superiors and then to the permanent head of the whole government department. His arguments were ignored and he was severely reprimanded for breaking the chain of official responsibility. He brooded over the matter and collected still more evidence to fortify his case. Then, over the heads of his superiors, he wrote direct to the cabinet minister responsible for the department. To communicate in this way is a heinous offense for a permanent civil servant in England. He was suspended from his post. Because of the large sum of money involved, however, the minister had the question thoroughly investigated. S. was completely vindicated and the rebate was abolished forthwith. He was summoned to a personal interview with the minister. Later he was officially thanked for his services to the country. By implication his superiors were sharply rebuked. His vindication seems to have been the crucial point in unbalancing his judgment. It was at this point that he was transformed from a paranoid personality into a true paranoic.

S. was offered the alternatives of reinstatement in his former post or transfer to a more congenial one, with good prospects of early promotion in either choice. Against earnest advice, however, he insisted on resigning his position in the Civil Service, together with his rights to pension and gratuity. He was then 49 years old. During his period of suspension he had studied the whole background of what he called the Rebate Fraud. He had conducted extensive researches into the historical and legal basis in England of taxation, revenue, the issue of money and banking. His earlier studies enabled him to do this competently. He came upon the fact that Charles the Second had, contrary to the letter of the law, granted a right of seigniorage upon the coinage to his mistress Barbara Villiers, Duchess of Cleveland. Subsequently Charles had sold the right to issue money, in the form of banknotes and checks, to a group of financiers in the City of London. From these facts S. inferred that the whole monetary and banking system of the country was illegal and a fraud on Parliament. This situation he originally termed the Money Fraud and afterwards the Royal Fraud. (In parenthesis it may be noted that S's historical statements are, of course, correct but that the flaw in his argument is an over-rigid acceptance of legal enactments and a neglect of changes in the social and economic structure of the country.) In order to be free to write letters that would expose this fraud he resigned his post in the Civil Service. His success in getting the Rebate Fraud rectified by a letter to the responsible minister caused him to believe that letters and memoranda to the King, the Cabinet and the leading Opposition members would similarly bring about a rectification of the Royal Fraud.

For some time S. maintained himself and his sister on his quite considerable savings. Afterwards he sold his house and they went to live in rooms. He poured out a stream of communications about the Royal Fraud but the polite and non-committal acknowledgements were hardly encouraging. Meanwhile he extended his researches over a much wider field including ancient and medieval history, archaeology and anthropology. Suddenly a blinding truth dawned on him, parallel, he felt, to the discoveries of Archimedes, Newton and Einstein. Money from its inception as barter in the neolithic period had rested on deceit and misunderstanding. This was the real or grand Money Fraud beside which Charles the Second's Royal Fraud had been a mere peccadillo. Money was a fraud because goods are essentially incommensurable. The attempt to make them commensurable was the basic cause of all the ills of society from the remote past to the present. The solution to all political and economic difficulties was the immediate abolition of money. The basic law of human relationships was human fraternity and free distribution in a free world society.

S. now began to bombard the Royal Family, the Cabinet and other members of Parliament, foreign ambassadors, scientific societies, public bodies of all sorts and prominent individuals with innumerable letters and memoranda. These were all typed or duplicated by an agency so that the procedure was very costly. His communications were all clearly written and well argued but hardly distinguished by the tact necessary to win support for a cause. For example one of his letters to the King declared: "The root of the world's troubles is the Money Fraud for which the British Hereditary Monarchy provides the chief cover and the real obstacle in the way of rectification. Satan could not have two better agents than the present King and Queen."

In addition to producing this flood of letters and memoranda S. wrote a most erudite book in support of his theories, called The Creation of a New Civilization. It comprised 100,000 words in 34 chapters. The book was in accord with the highest tradition of scholarship, lucidly presented and closely argued. No defect of reasoning was at any point discernible. Only sharp vigilance could detect the essential weakness in S's arguments, for example, his mistaken concept of measurement or his neglect of the psychological and sociological conditions on which work, demand and exchange depend. His defects lay in judgment, in awareness of likelihood and in feeling for what is appropriate. His deficient awareness of likelihood was especially evident in his attempt to deal with the problems of incentives that would immediately arise if money were abolished and free distribution substituted. It was also evident in his notion that his theories merely

had to be publicized to win general support. The book was suffused with strong moral feeling, although he tacitly rejected in it many of the tenets of the strict religious creed he had once so unwaveringly maintained. A prudish outlook on sexuality survived in his reiterated indignation that Charles the Second's fraud was originally in the interests of his mistress. One curious feature, in view of his brilliant mathematical attainments, was his complete rejection of that discipline as a tool towards the establishment of truth: "Careful scrutiny of the foundations of mathematics has revealed the severe limitations in its abstractive nature. In penetrating more deeply into the essence of physical or social phenomena, truths are reached which cannot be expressed in mathematical terms. The statements of Jeans about the mathematical nature of the universe are inadequate because more profound truths control and condition such formulations. Truth transcends mathematics both in depth and scope. Mathematics can be and is used in the service of Satan. There is a hidden vice in the science itself."

When S. found that his letters and memoranda continued to receive only polite refusal or non-committal acknowledgement, he decided to appeal directly to the public by addressing open-air audiences. His listeners did not stay long. Needless to say, no publisher was prepared to accept his book. He resolved openly to flout the law so as to draw attention to his ideas. He thought that if he were arrested he would figure before the public as a political martyr. He refused to pay rent or income tax, he deliberately incurred a bank overdraft and issued a number of bad checks. The matter of the rent finally ended in his being evicted from his rooms by court order. In court he addressed the judge on the Royal Fraud and the Money Fraud but was referred for satisfaction to a superior court. To the demands of the income tax and bank officials he replied with letters explaining his ideas and they thought it simplest to let the matter drop. In a frantic effort to get arrested he threw stones at the windows of a police-station but the police, when they ascertained the circumstances, did not wish to prosecute.

By the sixth year from S's resignation his funds were becoming very low. He began to make attempts to secure employment but his age and the dubious circumstances of his leaving the Civil Service were against him. In desperation he wrote further letters to the Royal Family, the Cabinet and others demanding financial support, not as a charity but as a fundamental right in view of his discoveries. At this time he began to express delusions of personal persecution; an attempt was being made to murder his sister and himself by secret-police methods in order to stifle the truth. Hitherto his delusions of persecution and grandeur had alike been impersonal. The object of persecution was humanity itself; the grandeur was that of his discoveries, not of himself. The personal delusions were definitely secondary to the impersonal ones, being long subsequent in time to them and logically dependent on them. They were also considerably more amenable to reasoned argument.

At the age of 56 S. was completely destitute. The public assistance authorities were invoked and they approached his relatives. He went to live with his elder brother. The latter managed by a stratagem to have him examined psychiatrically. Eventually he was removed to a mental hospital as being in need of care and protection. S. vigorously protested his sanity and interpreted his commitment in terms of the delusions of personal persecution just named. He carefully studied the law relating to mental illness and agitated for his discharge. He was pleasant in manner and, as he believed they would facilitate his release, cooperative in all investigations conducted, including psychological tests. The latter confirmed his high ability (Wechsler-Bellevue I.Q. 145) and showed no evidence of intellectual deterioration. His mathematical knowledge, however, had become decidedly rusty. In personality tests, such as the M.M.P.I., his scores were entirely within normal limits. The remaining members of S's family were indignant with the elder brother for having brought about his commitment and pressed for his discharge. The leading figure in this was the unmarried sister that S. had maintained; she fully accepted his theories about money, in addition to having a semi-delusional system of her own about vegetarianism. Four months after his admission S. was discharged into the care of a married sister.

His short stay in hospital brought about a number of changes in S. The commitment was itself a profound shock that occasioned a certain amount of self-appraisal. He had many opportunities to discuss his ideas and procedures with psychiatrists and psychologists. While of course no attempt was made to refute his basic theories it was suggested that winning support for them would necessarily be slow and that less spectacular methods might succeed better in the long run. It was also suggested that his ideas of personal persecution were unjustified. It was hardly expected that such suggestions would have any effect at all but they appear to have had a definite influence upon him. A psychiatric social worker, in discussing his occupational prospects, indicated that it might be best to content himself with something much below his past level. He took this so literally that soon afterwards he began going out each day, quite contrary to hospital regulations, to work as a farm-hand a few miles away. He read voraciously, especially on nuclear physics. His delusional system underwent a further development. He became convinced that when the basic law of free distribution in a free world society came into operation new human energies would be released, allied to but transcending atomic energy. The relationship between atomic energy, the purpose of the universe and the motives of human beings became of absorbing interest to him.

After leaving hospital he obtained a clerical job in the transport industry, greatly below his ability and qualifications. He gave all his spare time to

reading advanced physics. Then he began to write his second book, on Atomic Energy and the New Civilization. When last seen, three years after his discharge, he still held this job and was in process of completing his book. He had in no way abandoned his views on the Royal Fraud and the Money Fraud but they had become integrated into a wider system connected with atomic energy. He no longer practiced his technic of pestering prominent individuals and public bodies, because he had decided it was futile. He had also decided that further attempts at flouting the law would be useless. His delusions of personal persecution had apparently disappeared.

In the annals of paranoia the special interest of S. as a case rests on the impersonal, scholarly character of his delusions, their steady development from stage to stage and the way a striking justification disorganized his judgment of likelihood. The personal vengefulness which characterized the classic case of the merchant Kohlhase[4] and the sexual guilt which was so prominent a feature in those other classic cases, the head-teacher Wagner[5,6] and the seminarist Arnold[7] were alike absent. S. had of course masturbated a certain amount throughout his adult life but on this question he showed only culturally conditioned embarrassment, no exceptional feelings of guilt. He impressed those that examined him as having a weak sexual drive and, though his prudery might seem to indicate otherwise, as not being greatly interested in sexual matters. It would be possible by selection and symbolic interpretation to fit the facts of his paranoic reaction to a hypothesis of latent homosexuality[2] but there was no demonstrable evidence of it. Essential influences in the development of his disorder seem to have been his upbringing in a culturally deviant religious sect, his long history of occupational frustration, and the absence of checking or discussion of his ideas entailed by his lack of social contacts. These and similar relevant factors in his biography have operated on others without the same consequences. It is difficult to avoid the conclusion, despite the absence of recorded behavioral disorder in his pedigree, that in S. such factors played on a cerebrum already predisposed to a paranoic reaction.

Summary

1. The development of a case, unanimously diagnosed by several independent psychiatrists as pure paranoia, is traced through the stages of apparently normal personality, difficult personality, paranoid personality and true paranoic.

2. The patient was a British civil servant of exceptionally high ability and brilliant mathematical attainments. The crucial point at which he was transformed from a paranoid personality to a true paranoic is judged to have been his vindication against his superiors in regard to a malpractice he had exposed.

3. The impersonal character of his delusions is stressed and the erudite book he wrote to expound them is described.

4. The circumstances of his commitment to a mental hospital, subsequent discharge and partial readjustment are outlined and the etiological factors in the case discussed.

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REFERENCES

1. Bumke, O.: Lehrbuch der Geisteskrankheiten, 2nd ed. *Bergmann,* Munich, pp. 554-584, 1924.
2. Bonner, H.: The problem of diagnosis in paranoic disorder. *Amer. J. Psychiat.,* 107:677, 1951.
3. Kraepelin, E.: Manic-depressive Insanity and Paranoia, trs. R. M. Barclay, *Livingstone,* Edinburgh, pp. 207-277, 1921.
4. Burkhardt, C. A. H.: Der Historische Hans Kohlhase und Heinrich von Kleist's Michael Kohlhaas. *Vogel,* Leipzig, 1864.
5. Gaupp, R.: Zur Psychologie der Massenmorde: Hauptlehrer Wagner von Degerloch. *Springer,* Berlin, 1914.
6. Gaupp, R.: Der Fall Wagner. Ein Katamnese zugleich ein Beitrag zur Lehre von der Paranoia. *Z. ges. Neurol. Psychiat.,* 60:312, 1920.
7. Kehrer, F.: Der Fall Arnold. Studie zur neueren Paranoialehre. *Z. ges. Neurol. Psychiat.,* 74:155, 1922.

Hyperostosis Frontalis Interna

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While reviewing the pneumoencephalograms carried out over a period of five years at a University Hospital, a small number of the films were noted to present the picture of hyperostosis frontalis interna. This type of intracranial calcification has been interpreted by some as pathological significance. In fact, the so-called Stewart-Morel Syndrome consists of a patient with headaches, obesity and psychiatric symptoms in the presence of hyperostosis frontalis interna. Because in this small series we have the additional help of the pneumoencephalographic findings to add to any interpretation, these cases are reported.

The skull films of 510 patients were reviewed. Hyperostosis frontalis interna was reported in seventeen (3.3%) of this group. Young[1] found an incidence of 5% in all skulls he examined roentgenographically, and Troger[2] stated this finding occurs in 1-40% of our population. Moore,[4] in a review of 96,000 skull films, reported an incidence of 1.2%.

Most authors state that this bony overgrowth occurs predominately in women. Four of the cases in this series were in males and thirteen were in females. Moore[4] found that 97.2% of his patients with the hyperostosis frontalis interna were females.

The excess bone arises from the inner table on both sides of the mid-line. It is found principally in the frontal bone and presents a scalloped appearance.

Twelve (70.6%) of this group had a convulsive disorder. Three of the patients were examined because of headache; one had a right hemiparesis secondary to trauma and one an organic brain syndrome. The incidence of this x-ray picture with an accompanying convulsive state is variously reported from 8.5% (Moore[4]) to 35.3% (Carr[5]). In the total group of 510 patients from which these cases of hyperostosis frontalis interna were separated, 355 were studied because of a convulsive picture. Thus 69.6% of the patients whose skull x-rays were reviewed had seizures.

The encephalographic findings were interpreted as follows:

1) Normal encephalogram—7.
2) Signs of cerebral atrophy, either localizing or general—5.
3) Unsuccessful encephalograms—5.

There were two tumors, both meningiomas, one of which had been removed two years previous to the reported air study. Neither was in a location to confuse the skull changes in people with tumors with the picture of hyperostosis frontalis interna. Reider[3] reported the association of hyperostosis frontalis interna with degenerative brain disease in two cases.

This group of patients with overgrowth of bone from the inner table of the frontal region is too small to draw any definite conclusions from. A high percentage (70.6%) did have a convulsive disorder which is larger than the figures quoted by other writers on the subject. Less than half of the group was found to have a normal pneumoencephalogram. Although cerebral changes were noted on the air studies of 30% of the group, no correlation can be made as to the relationship of the two findings.

BIBLIOGRAPHY

1. Young, B. P.: The Skulls, Sinuses and Mastoids. *Year Book Publisher.*
2. Troger, et al.: Hyperostosis Calverii Interna. *California & West. Med.*, 51: 384, 1939.
3. Reider, N.: Hyperostosis Frontalis Interna and Degenerative Brain Disease. *J. Mt. Sinai Hospital*, 5: 511, 1938.
4. Moore, S.: Hyperostosis Frontalis Interna. *Surg. Gyn. & Obstetrics*, 61: 345, 1935.
5. Carr, A. D.: Neuropsychiatric Syndromes Associated with Hyperostosis Frontalis Interna. *Arch. Neurol. & Psychiat.*, 35: 982, 1936.
6. Perkins, et al.: Hyperostosis Frontalis Interna. *Psychiatric Quart.* 12: 341, 1938.
7. Grollman, A., et all.: Metabolic Craniopathy. *JA MA*, 126: 213, 1944.

Book Reviews

ANATOMY OF THE NERVOUS SYSTEM. By Ranson and Clark. W. B. Saunders Company. 581 p. $8.50.

Here is presented a long awaited, up to date revision of a textbook of neuroanatomy that has withstood the test of time and has grown in the regard of anatomists and clinicians. The text has been enlarged by the addition of 41 pages and, along with this, there is an increase of 13 pages of bibliography. This expansion of the text has incorporated the latest significant advances in neuroanatomy and the latest development in neurophysiology in a manner in which they may be used by the clinician.

Doctor Clark continues to have the very important chapter on clinical illustrations that has been found so useful by the student of neuroanatomy. These illustrations are of great value to the students of neuroanatomy because of their practicality and the method of their presentation. The chapter on brain sections and the laboratory outline of neuroanatomy will be particularly useful to the student as he undertakes the initial chore of getting the anatomical relations of the nervous system firmly fixed in his mind for future use.

Francis J. Braceland, M.D.

THE NERVOUS TRANSMISSION. By Ichiji Tasaki. Charles C. Thomas.

This monograph is a well written, concise, carefully illustrated review of experiments on the latest theory of the transmission of nerve impulses. The statements made are illustrated by detailed descriptions of experimental work which has been done with isolated nerve fibers and there are additional illustrations of the experimental evidence to hand in order that these concepts may be better understood.

The beginning chapters sets forth the accepted fundamental concepts of nerve physiology. The second and third chapters consider the electric properties of the node of Ranvier and its role in the transmission of impulses along the nerve fibers. It is the author's contention, proven by experimental evidence, that an electrical current above a certain strength sent into a nerve fiber elicits action currents 5 to 7 times as high as the strength of the stimulating current. A node of Ranvier is the critical site of the development of action currents and the nerve impulses travel along the nerve fiber in a saltatory manner from each successive node of Ranvier, restimulating its neighbor.

The fourth chapter deals with the properties of the nerve fiber carrying an impulse, particularly with reference to the electrical resistance of the plasma membrane, impedance changes during activity, membrane action current, and the electrical field produced in the conducting medium by a nerve impulse. The fifth chapter discusses the myelin sheath and the sixth, seventh, and eighth chapters consider the effects on nerve impulse transmission of refractoriness, narcosis and electrotonus. The ninth and final chapter discusses in detail the application of experimental evidence to the transmission of an impulse over the nerve trunk.

There are three appendices which describe the technique of preparing a single vertebrate nerve fiber, nervous transmission as a mathematical problem, and some implications of the saltatory nature of transmission. There is a good bibliography appended to the text.

Francis J. Braceland, M.D.

MUSIC THERAPY by Edward Podolsky, M.D., Philosophical Library, New York. $6.00.

It is probable that this book will after a short time be one of the most popular books in the field of music therapy. It is the work of a group of experts in the field and, though it suffers from the same difficulties of any cooperative venture in writing, namely unevenness and overlapping, it is nonetheless a worthwhile volume. Aside from the intrinsic worth of the book, there is a thirst for information about the subject and, inasmuch as this particular volume has a general appeal, it will be readily accepted.

It is interesting to note that until five or ten years ago any type of music used in hospitals was thought to be of therapeutic value. This book points up a trend which is now taking place in the field. Actually, music cannot be accepted by the medical profession until its worth has been proven on a research level and the problem of music therapy is one which can be solved only by the cooperation of psychiatrists, psychologists and musicians. Thus far there have been too many sweeping generalizations as to the effectiveness of music but in this book a large amount of space is devoted to research projects which indicate that music therapy is now beginning to justify its own existence in scientific terms.

Although it may seem ungracious to criticize, there are several chapters in the book in which statements are made that undesirable moods can be changed by playing specific pieces of music. Are these lists of music really of value to anyone except perhaps the player? The style, the mood, the tempo, familiarity with selection, etc., are not taken into account. There are other rather sweeping generalizations but the actual worth of the book lies in the chapters on research. This material is worthy of consideration and may ultimately lead to a better understanding of music as therapy.

Francis J. Braceland, M.D.

DIAGNOSTIC TESTS IN NEUROLOGY, Robert Wartenberg, M.D., First Edition, 1953. Chicago: The Year Book Publishers, Inc. 228 pages, illustrated.

According to the author this book is written for the general practitioner as a supplement to the text-

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books of neurology and as a postgraduate refresher course in neurological diagnosis. It could very well serve the medical student, intern and resident as a ready reference work where very lucid, common sense explanations of most of the neurological signs and tests could be found. The teacher of neurology will also find much in the concise volume to aid him in answering the bewildering barrage of questions from junior and senior students.

The introduction emphasizes the use of clinical diagnostic tests rather than laboratory examinations, with a strong plea for a return to the use of several senses before resorting to procedures that may be time consuming, expensive, possibly harmful, and occasionally misleading.

The main portion of the book is divided into seven sections: cranial nerves, peripheral nerves, pyramidal system, extrapyramidal system, cerebellar system, sensory system and vasomotor-trophic system. Each section consists of a series of tests that thoroughly explore the various functions, both normal and pathological, of the system, with concise, simple explanations of the phenoman demonstrated. Dr. Wartenberg is particularly adept at avoiding involved neuroanatomical and neurophysiological detail that would tend to confuse and discourage the busy practitioner who wants a ready answer without too many whys and wherefors.

The text is profusely illustrated with photographs of patients demonstrating the pathological signs described.

The author has carefully avoided attaching men's names to tests. In fact, the only one mentioned is the Babinski reflex, all others have descriptive titles such as Doll's eye test, See-saa test in oculomotor paralysis, wrist drop test, etc.

No bibliography is included but there are two complete indices, a special index of morbid conditions—pertinent tests and a general index.

The book is recommended for all general practitioners who have an interest in trying to simplify and understand the neurological examination and to those teachers of neurology who desire to make their teaching more understandable to the uninitiated.

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LIVING WITH A DISABILITY. Howard A. Rusk, M.D., and Eugene J. Taylor. The Blakiston Company, Pp. 207. $3.50.

This book is a most remarkable connection of 282 photographs with explanatory text. It illustrates simple methods and self-help devices for meeting effectively the handicaps of the physically disabled. Beginning with general advice on adjusting to a disability, and the evaluation of devices for assistance, the authors proceed to practical consideration of daily activities ranging from the vital function of eating, through the less necessary but still important recreational sphere, not neglecting the possibilities of overcoming the difficulties of housework and gainful employment. The information ranges from simple hints on the management of the trivia of everyday life to house layouts. Where expensive devices are recommended, the authors also include mention of cheaper if less efficient substitutes. Making the most of what one has, both materially and of one's own potentialities, is constantly stressed.

Every physically handicapped person can read this book with profit and it should be a standard reference for everybody who deals with disabled persons. It is the result of a research project by the New York Institute of Physical Medicine and Research and it is well and rightly designed to bring hope and help to those who need it.

Milton H. Erickson, M.D.

SEMINARS IN RORSCHACH TEST

The Department of Psychology, University of Chicago, will conduct two workshop seminars in the Rorschach Test, July 6-10, 1954, and July 12-16, 1954 (inclusive). Workshop I, Basic Processes, will provide a grounding in fundamentals and procedure in obtaining the test record. Representative responses will be illustrated, their scoring clarified, with especial reference to their inter-relations in shaping the whole personality structure.

Workshop II, Advanced Clinical Interpretation, will consider the ego, anxiety, and the individual's psychological reserves as treatment potential.

For information as to admission, fees, or academic credit arrangements, write to the Executive Secretary, Department of Psychology, The University of Chicago, Chicago 37, Illinois.

RESIDENCIES IN V. A. HOSPITAL

The Veterans Administration Hospital, Lyons, New Jersey, has available residencies in Psychiatry for a one to three year period which are fully accredited by the American Board of Psychiatry and Neurology. The training program consists of lectures, conferences and seminars under the direction of the Department of Psychiatry, New York Medical College, and offers intensive training, both intramurally and through rotation in special hospitals and clinics in the adjacent area. There is, in addition, a series of extensive guest lecturers as well as an Annual Institute at the hospital. Training may commence at any time.